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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Apr 08  "Ask CAS" for self-help around the clock
 NEWS  3  Apr 09  BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS  4  Apr 09  ZDB will be removed from STN
 NEWS  5  Apr 19  US Patent Applications available in IFICDB, IFIPAT, and
IFIUDB
 NEWS  6  Apr 22  Records from IP.com available in CAPLUS, HCAPLUS, and
ZCAPLUS
 NEWS  7  Apr 22  BIOSIS Gene Names now available in TOXCENTER
 NEWS  8  Apr 22  Federal Research in Progress (FEDRIP) now available
 NEWS  9  Jun 03  New e-mail delivery for search results now available
 NEWS 10  Jun 10  MEDLINE Reload
 NEWS 11  Jun 10  PCTFULL has been reloaded
 NEWS 12  Jul 02  FOREGE no longer contains STANDARDS file segment
 NEWS 13  Jul 22  USAN to be reloaded July 28, 2002;
                  saved answer sets no longer valid
 NEWS 14  Jul 29  Enhanced polymer searching in REGISTRY
 NEWS 15  Jul 30  NETFIRST to be removed from STN
 NEWS 16  Aug 08  CANCERLIT reload
 NEWS 17  Aug 08  PHARMAMarketLetter(PHARMAML) - new on STN
 NEWS 18  Aug 08  NTIS has been reloaded and enhanced
 NEWS 19  Aug 19  Aquatic Toxicity Information Retrieval (AQUIRE)
                  now available on STN
 NEWS 20  Aug 19  IFIPAT, IFICDB, and IFIUDB have been reloaded
 NEWS 21  Aug 19  The MEDLINE file segment of TOXCENTER has been reloaded
 NEWS 22  Aug 26  Sequence searching in REGISTRY enhanced
 NEWS 23  Sep 03  JAPIO has been reloaded and enhanced
 NEWS 24  Sep 16  Experimental properties added to the REGISTRY file
 NEWS 25  Sep 16  Indexing added to some pre-1967 records in CA/CAPLUS
 NEWS 26  Sep 16  CA Section Thesaurus available in CAPLUS and CA
 NEWS 27  Oct 01  CASREACT Enriched with Reactions from 1907 to 1985
 NEWS 28  Oct 21  EVENTLINE has been reloaded
 NEWS 29  Oct 24  BEILSTEIN adds new search fields
 NEWS 30  Oct 24  Nutraceuticals International (NUTRACEUT) now available on
STN
 NEWS 31  Oct 25  MEDLINE SDI run of October 8, 2002
 NEWS 32  Nov 18  DKILIT has been renamed APOLLIT
 NEWS 33  Nov 25  More calculated properties added to REGISTRY
 NEWS 34  Dec 02  TIBKAT will be removed from STN
 NEWS 35  Dec 04  CSA files on STN
 NEWS 36  Dec 17  PCTFULL now covers WP/PCT Applications from 1978 to date
 NEWS 37  Dec 17  TOXCENTER enhanced with additional content
 NEWS 38  Dec 17  Adis Clinical Trials Insight now available on STN
 NEWS 39  Dec 30  ISMEC no longer available
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 NEWS EXPRESS  December 31 CURRENT WINDOWS VERSION IS V6.01a,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
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FILE 'HOME' ENTERED AT 13:52:58 ON 06 JAN 2003

=> file medline caplus cancerlit embase biosis
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                     0.21       0.21

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=> s liquid (w)droplet(w) aerosol
L1          11 LIQUID (W) DROPLET(W) AEROSOL

=> duplicate remove
ENTER L# LIST OR (END):l1
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, EMBASE, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L1
L2             6 DUPLICATE REMOVE L1 (5 DUPLICATES REMOVED)

=> d l2 1- ibib,abs
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L2   ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2001:507506  CAPLUS
DOCUMENT NUMBER:          135:97468
TITLE:                    .gamma.-IFN liquid-droplet
```

**aerosol** and method
INVENTOR(S): Emlen, J. Woodruff; Van Vlasselaer, Peter
PATENT ASSIGNEE(S): Intermune Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001049260 | A2 | 20010712 | WO 2000-US42831 | 20001222 |
| WO 2001049260 | A3 | 20020207 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2001043906 | A1 | 20011122 | US 2000-747383 | 20001222 |
| BR 2000016884 | A | 20021001 | BR 2000-16884 | 20001222 |
| NO 2002003135 | A | 20020823 | NO 2002-3135 | 20020627 |

PRIORITY APPLN. INFO.: US 1999-173926P P 19991230
WO 2000-US42831 W 20001222

AB A **liq.-droplet aerosol** compn. for delivery to a patient's respiratory tract is disclosed. The aerosol is formed by placing an aq. .gamma.-IFN soln. having stabilizing and dispersing components against a plate having defined-size openings, and forcing the soln. through the openings under conditions effective to form aq. droplets having a vol. mean diam. in one or more of a no. of selected sizes in the 1-10 .mu. size range. The aerosol has the desired-size droplets and a .gamma.-IFN biol. activity and mol. size distribution substantially the same as that of the aq. .gamma.-IFN soln. Also disclosed is a method of administering to a selected region of a patient's respiratory tract, an amt. of human .gamma.-IFN having a known, selected gamma-interferon biol. activity and mol. size distribution.

L2 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
ACCESSION NUMBER: 1999:469947 CAPLUS
DOCUMENT NUMBER: 131:119807
TITLE: Performance evaluation of the sampling head and annular kinetic impactor in the Savannah River Site alpha continuous air monitor
AUTHOR(S): Chen, Bean T.; Hoover, Mark D.; Newton, George J.; Montano, Sandra J.; Gregory, Donald S.
CORPORATE SOURCE: Health Effects Laboratory Division, National Institute for Occupational Safety and Health, Morgantown, WV, 26505, USA
SOURCE: Aerosol Science and Technology (1999), 31(1), 24-38
CODEN: ASTYDQ; ISSN: 0278-6826
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Evaluation and testing of the Savannah River Site (SRS) impactor-type

alpha continuous air monitor (CAM) to det. device particle delivery and collection efficiency using fluorescence-labeled, polystyrene latex spheres and **liq. droplet aerosols** is described. Particle sampling efficiency through the dome-shape sampling inlet for particles with aerodynamic diams. of 6.2 and 10 .mu.m was 98% at 20 cfm (566 L/min), 90% at 32 cfm (906 L/min), and 87% at 40 cfm (1132 L/min) sampling flow rates. Internal delivery efficiency through the CAM was >94% at 20 and 32 cfm for 0.5-, 1.1-, 2.2-, and 3.2-.mu.m particles and >90% for 6.2 .mu.m particles. For 10-.mu.m particles, the internal delivery efficiency was 91% at 20 cfm and decreased to 83% at 32 cfm and 77% at 40 cfm. The 50% cutoff aerodynamic diam. for the impactor was 3.2 .mu.m at 20 cfm, 2.6 .mu.m at 32 cfm, and 2.3 .mu.m at 40 cfm. For a typical radioactive aerosol in the workplace (activity median aerodynamic diam. = 5 .mu.m with a geometric std. deviation of 2), these cutoff diams. provided collection efficiencies of 74% at 20 cfm, 83% at 32 cfm, and 87% at 40 cfm. The normal grease layer of 1.5 mg routinely applied to the planchet of the SRS CAM was adequate to quant. retain all collected particles with diams. .ltoreq.3.2 .mu.m at flow rates of 20, 32, and 40 cfm. For particle sizes of 6.2 and 10 .mu.m, .apprx.80-85% of particles were retained on the impactor planchet; 15-20% were re-entrained into the exhaust airstream due to particle bounce. SRS CAM delivery and collection efficiencies can be combined to yield overall efficiencies to detect airborne actinide aerosols as a function of particle size. For 6.2 and 10 .mu.m aerodynamic diam. particles, total collection efficiency of the SRS CAM at 20, 32, and 40 cfm exceeded the conservative assumption of 50% efficiency for Pt particle collection traditionally used at SRS.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:372271 CAPLUS
DOCUMENT NUMBER: 129:117091
TITLE: Sampling and conditioning of gas containing liquids in droplet or aerosol form
AUTHOR(S): Mayeaux, Donald P.
CORPORATE SOURCE: A+ Corporation, Prairieville, LA, 70769, USA
SOURCE: Proceedings of the Annual ISA Analysis Division Symposium (1998), 31, 129-137
CODEN: ANDIEY; ISSN: 1050-6527
PUBLISHER: Instrument Society of America
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This presentation addresses problems assocd. with sampling gas which contains liq. in droplet or aerosol form. By elimination of entrained liq. at prevailing process conditions, gas compn. changes are avoided. Techniques to prevent condensation from occurring after the gas sample is extd. are also discussed.

L2 ANSWER 4 OF 6 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 92209411 MEDLINE
DOCUMENT NUMBER: 92209411 PubMed ID: 1555522
TITLE: Two-week aerosol inhalation study in rats of ethylene oxide/propylene oxide copolymers.

COMMENT: Erratum in: Drug Chem Toxicol 1992;15(3):269-70
AUTHOR: Ulrich C E; Geil R G; Tyler T R; Kennedy G L Jr; Birnbaum H
A
CORPORATE SOURCE: International Research and Development Corporation, Mattawan, MI 49071.
SOURCE: DRUG AND CHEMICAL TOXICOLOGY, (1992) 15 (1) 15-31.
Journal code: 7801723. ISSN: 0148-0545.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205
ENTRY DATE: Entered STN: 19920515
Last Updated on STN: 19920515
Entered Medline: 19920504

AB Previous studies have shown that aerosols of an ethylene oxide/propylene oxide copolymer (UCON 50-HB-5100) produced an inflammatory response in lungs of rats in short-term repeated exposures at relatively low concentrations. This study was carried out on related polyalkylene glycols (EO/PO copolymers) to determine if similar effects would occur upon short-term repeated exposure. Rats were treated by whole body **liquid droplet aerosol** exposures of six hours per day, five days per week for two consecutive weeks to each of five EO/PO copolymers. The exposure level for the positive control (UCON 50-HB-5100) was 55 mg/m3, while the remaining 4 test copolymers were evaluated at 100 mg/m3. Each exposure group consisted of ten male albino rats. After three exposures, nine of ten rats exposed to UCON 50-HB-5100, and six of ten rats exposed to UCON 50-HB-2000 had died. At necropsy, congestion, consolidation and red discoloration of the lungs were noted. A moderate to severe alveolitis, characterized by intraalveolar edema, hemorrhage and fibrin deposition, was observed after five days of exposure. At necropsy, these rats exhibited elevated lung weights and similar macroscopic and microscopic lesions. Rats exposed to the other test materials (UCON 75-H-1400, Pluronic L17R1, Pluronic L31, and Pluronic L64) survived with essentially no signs of toxicity through the ten exposure days. Body weights, organ weights, hematological evaluation, pharmacotoxic signs, and macroscopic and microscopic evaluation after necropsy were similar between groups and when compared to the negative control group. Only a slight alveolitis was noted after two weeks of exposure which subsided by two-weeks post exposure.

L2 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1987:69552 CAPLUS
DOCUMENT NUMBER: 106:69552
TITLE: The behavior of **liquid droplet aerosols** in an APS 3300
AUTHOR(S): Griffiths, W. D.; Iles, P. J.; Vaughan, N. P.
CORPORATE SOURCE: Occup. Med. Hyg. Lab., Health Saf. Exec., London, NW2 6LN, UK
SOURCE: Journal of Aerosol Science (1986), 17(6), 921-30
CODEN: JALSB7; ISSN: 0021-8502
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Monodisperse liq. and solid polystyrene latex (PSL) aerosols behaved in a significantly different manner in an Aerodynamic Particle Sizer (APS) 3300. The results were compared with those of other recent investigations

with a fair degree of agreement. The APS measurements indicated a decrease of the expected aerodynamic diam. of all of the liq. aerosols tested. This decrease might be dependent on the viscosity and diam. on generation of the drop. Monodisperse PSL should be used to calibrate the APS throughout its operating range, instead of a liq. aerosol.

L2 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1977:489845 CAPLUS
DOCUMENT NUMBER: 87:89845
TITLE: Critical review of the USCG report by Raj et al (1974)
on spills of liquid anhydrous ammonia on to water, with an alternative assessment of the experimental results
AUTHOR(S): Griffiths, R. F.
CORPORATE SOURCE: Saf. Reliability Dir., UKAEA, Culcheth/Warrington, UK
SOURCE: U. K. At. Energy Auth., Saf. Reliab. Dir., [Rep.] SRD (1977), SRD R 67, 17 pp.
CODEN: UKSRAP
DOCUMENT TYPE: Report
LANGUAGE: English
AB A polemic. the P. K. Raj (1974) report (NTIS AD 779400) concerning liq. NH3 spills from refrigerated storage tanks and the release of NH3 from them as a pure undild. vapor is challenged on the grounds that it is incompatible with exptl. measurements. NH3 is released as a plume contg. both vapor and **liq. droplet aerosol**, by virtue of which it is rendered nonbuoyant.

=> s lung (w)delivery (w) cytokines
L3 0 LUNG (W) DELIVERY (W) CYTOKINES

=> s lung (s) delivery (s) cytokines
L4 259 LUNG (S) DELIVERY (S) CYTOKINES

=> s aerosol (s) composition
L5 8004 AEROSOL (S) COMPOSITION

=> s l4 and l5
L6 0 L4 AND L5

=> s aerosol
L7 127142 AEROSOL

=> s l4 and l7
L8 42 L4 AND L7

=> duplicate remove l8
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, CANCERLIT, EMBASE, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L8
L9 17 DUPLICATE REMOVE L8 (25 DUPLICATES REMOVED)

=> d l9 1- ibib,abs
YOU HAVE REQUESTED DATA FROM 17 ANSWERS - CONTINUE? Y/(N):y

L9 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:71808 CAPLUS
DOCUMENT NUMBER: 136:123657
TITLE: Modulated release particles for drug delivery to lungs

INVENTOR(S): Adjei, Akwete L.; Zhu, Yaping; Cutie, Anthony J.; Sun, John Z.
PATENT ASSIGNEE(S): Aeropharm Technology Incorporated, USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002005730 | A1 | 20020124 | WO 2001-US41120 | 20010625 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-219051P P 20000718
US 2000-702894 A 20001031

AB A polymeric construct is disclosed. The construct comprises a biodegradable ABA block copolymer (e.g., polyglycolide-polylactide) having a selected drug assocd. therewith. The drug thus present is provided in a slow release form. Thus, a polymer was obtained from polyglycolide-polylactide with PEG as the crosslinker. The particle size distribution anal. of the amylin-polymer compn. was detd.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:616197 CAPLUS
DOCUMENT NUMBER: 137:174934
TITLE: Modulated-release polysaccharide **aerosol** particles for lung delivery
INVENTOR(S): Zhu, Yaping; Stefanos, Simon G.; Kline, Lukeysha; Adjei, Akwete L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 9 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2002110539 | A1 | 20020815 | US 2001-784670 | 20010215 |
| WO 2002066077 | A2 | 20020829 | WO 2002-US3970 | 20020206 |
| WO 2002066077 | A3 | 20021024 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2001-784670 A 20010215
AB A polymeric construct for lung delivery comprises a polysaccharide vehicle
entrapping a selected medicament. A polysaccharide is present in an amt. of about 0.0000001-10% by wt. of the construct and it is selected from, e.g., alginic acid, various gums, cellulose, agar, carrageenan, gelatin, galacturonic acid, etc. The medicament entrapped within the construct is provided in a slow release form. The medicament is for example a protein or peptide having a mol. size of about 1-150 kD, selected from insulin, glucagon, LH-RH, deltirex, leuprolide, calcitonin, parathyroid hormone, TRH, growth hormone-releasing hormone, G-CSF, a cytokine, DNase, heparin, an oligonucleotide, a monoclonal antibody, a vaccine, etc. Depending upon
the concn. of the polymer drug release rates range from 5 min to several hours.

L9 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:616192 CAPLUS
DOCUMENT NUMBER: 137:159362
TITLE: Modulated-release polymeric silicate particles for lung delivery
INVENTOR(S): Zhu, Yaping; Adjei, Akwete L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2002110527 | A1 | 20020815 | US 2001-784671 | 20010215 |
| US 6485707 | B2 | 20021126 | | |
| WO 2002066009 | A1 | 20020829 | WO 2002-US3995 | 20020207 |
| WO 2002066009 | C2 | 20021205 | | |

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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2001-784671 A 20010215
AB A modulated-release **aerosol** formulation for lung delivery
comprises a polymeric silicate construct, e.g., silica gel or fumed silica
gel, having a selected medicament assocd. there with, and a fluid carrier for carrying and delivering the construct. The polymer is present in an amt. of about 0.000001-10% of the total wt. of the formulation. A medicament comprises a protein or peptide with a mol. size of about 1-150 kD, such as insulin, amylin, an interleukin, an interferon, heparin, a

thrombolytic, an antitrypsin, a hormone, a growth factor, an enzyme, etc.

L9 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:616191 CAPLUS
DOCUMENT NUMBER: 137:174932
TITLE: Modulated-release polysaccharide particles for lung delivery
INVENTOR(S): Zhu, Yaping; Stefanos, Simon G.; Kline, Lukeysha; Adjei, Akwete L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 10 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2002110526 | A1 | 20020815 | US 2001-784566 | 20010215 |
| US 6475468 | B2 | 20021105 | | |
| WO 2002066078 | A2 | 20020829 | WO 2002-US3971 | 20020206 |
| WO 2002066078 | A3 | 20021024 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-784566 A 20010215
AB A modulated (slow) release **aerosol** formulation comprises a particulate polysaccharide polymer, e.g., alginic acid, various gums, cellulose, gelatin, agar, carrageenan, gelatin, etc., having a selected medicament assocd. there with, and a fluid carrier for carrying and delivering the construct. The polymer is present in an amt. of about 0.000001-10% of the total wt. of the formulation. A medicament is, for example, a protein or peptide drug, such as insulin, amylin, glucagon, LH-RH, deltirex, leuprolide, gosorelin, nafarelin, octreotide, somatostatin, calcitonin, etc. A fluid carrier is selected from a propellant, air, carbon dioxide, nitrogen or a hydrocarbon. The **aerosol** is dispensed in a canister equipped with a metered dose valve.

L9 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:616190 CAPLUS
DOCUMENT NUMBER: 137:174931
TITLE: Modulated release particles for pharmaceutical lung delivery
INVENTOR(S): Adjei, Akwete L.; Zhu, Yaping
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2002110525 | A1 | 20020815 | US 2001-784556 | 20010215 |
| WO 2002066008 | A1 | 20020829 | WO 2002-US3992 | 20020207 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-784556 A 20010215

OTHER SOURCE(S): MARPAT 137:174931

AB A modulated release **aerosol** formulation is disclosed. The formulation comprises a polysaccharide polymer having a selected drug assocd., a fluid carrier for carrying and delivering the construct and a stabilizer. The stabilizer is selected from the group consisting of an amino acid e.g., a monoaminocarboxylic acid, a monoaminodicarboxylic acid and a diaminomonocarboxylic acid. The polysaccharide can be from alginic acid or a salt, e.g., guar gum, gum karaya, agar, carrageenan, and cellulose.

L9 ANSWER 6 OF 17 MEDLINE DUPLICATE 1

ACCESSION NUMBER: 2002696539 IN-PROCESS

DOCUMENT NUMBER: 22345302 PubMed ID: 12458152

TITLE: Pharmacological approaches for the discovery and development of new anti-inflammatory agents for the treatment of cystic fibrosis.

AUTHOR: Konstan Michael W; Davis Pamela B

CORPORATE SOURCE: Department of Pediatrics, Case Western Reserve University School of Medicine and Rainbow Babies and Children's Hospital, 11100 Euclid Avenue, 44106, Cleveland, OH, USA.

SOURCE: Adv Drug Deliv Rev, (2002 Dec 5) 54 (11) 1409-23. Journal code: 8710523. ISSN: 0169-409X.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals

ENTRY DATE: Entered STN: 20021217

Last Updated on STN: 20021217

AB Some of the most important pathobiology in cystic fibrosis occurs not as a direct result of impaired chloride transport, but the downstream consequences of defective CFTR function, particularly the **lung** infection and inflammation that ultimately takes the lives of most patients. Interrupting the vicious cycle of infection and inflammation is effective in slowing the course of the disease, and antibiotics have long been the staple of pulmonary therapy. However, limiting the inflammatory response in the CF **lung** is also effective. High dose ibuprofen clearly retards progression of **lung** disease, but also entrains adverse events that mar its therapeutic utility, so alternative anti-inflammatory agents are necessary. Because of the remarkable therapeutic success of ibuprofen, consideration should be given to finding less toxic alternatives. However, it is also appropriate to consider the mechanisms by which the inflammatory response occurs in the CF **lung**, and identify sites to interrupt it. Sites at which therapeutic intervention is possible are the neutralization of

**cytokines** such as tumor necrosis factor-alpha, interleukin (IL)-1beta, or IL-8 with specific antibodies or receptor antagonists, inhibition of the intracellular signaling cascades that result in cytokine production (for example, at the level of p38 MAP kinase), application of **cytokines** such as Il-10 that are themselves anti-inflammatory, or modulating the arachidonic acid cascade with inhibitors directed at leukotriene B(4). In addition, interventions designed to limit the consequences of the inflammatory response, such as protease inhibitors and reagents to limit the ill effects of DNA accumulation in airways, are in use. To limit adverse effect and concentrate the therapeutic effect, there may be value in targeting **delivery** of the therapeutic reagents to the inflamed site, either by specifically directing systemic **delivery** or by exploitation of the **aerosol** route. Treating the inflammatory response is important, for the data from the ibuprofen study show that the effects of anti-inflammatory therapy are additive or even synergistic with intensive conventional therapy and alter the rate of decline of pulmonary function, and therefore benefits for survival of patients with CF are to be expected.

L9 ANSWER 7 OF 17 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001245334 MEDLINE
DOCUMENT NUMBER: 21101774 PubMed ID: 11181627
TITLE: Methodology for the measurement of mucociliary function in the mouse by scintigraphy.
AUTHOR: Foster W M; Walters D M; Longphre M; Macri K; Miller L M
CORPORATE SOURCE: Department of Pulmonary and Critical Care Medicine, Duke University Medical Center, Durham, North Carolina 27710, USA.
CONTRACT NUMBER: ES-03810 (NIEHS)
HL-62641 (NHLBI)
SOURCE: JOURNAL OF APPLIED PHYSIOLOGY, (2001 Mar) 90 (3) 1111-7. Journal code: 8502536. ISSN: 8750-7587.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010510

AB The objective of the study was to develop a scintigraphic method for measurement of airway mucociliary clearance in small laboratory rodents such as the mouse. Previous investigations have characterized the secretory cell types present in the mouse airway, but analysis of the mucus transport system has been limited to in vitro examination of tissue explants or invasive in vivo measures of a single airway, the trachea. Three methods were used to deposit insoluble, radioisotopic colloidal particles: oropharyngeal aspiration, intratracheal instillation, and nose-only **aerosol** inhalation. The initial distribution of particles within the lower respiratory tract was visualized by gamma-camera, and clearance of particles was followed intermittently over 6 h and at the conclusion, 24 h postdelivery. Subsets of mice underwent lavage for evidence of tissue inflammation, and others were restudied for reproducibility of the methods. The aspiration and instillation methods of **delivery** led to greater distributions of deposited activity within

the **lungs**, i.e., approximately 60--80% of the total respiratory tract radioactivity, whereas the nose-only **aerosol** technique attained a distribution of 32% to the **lungs**. However, the **aerosol** technique maximized the fraction of particles that cleared the airway over a 24-h period, i.e, deposited onto airway epithelial surfaces and cleared by mucociliary function such that **lung** retention at 24 h averaged 57% for **delivery** by **aerosol** inhalation and > or =80% for the aspiration or intratracheal instillation techniques. Particle **delivery** methods did not cause **lung** inflammation/injury with use of inflammatory cells and chemoattractant **cytokines** as criteria. Scintigraphy can discern particle deposition and clearance from the lower respiratory tract in the mouse, is noninvasive and reproducible, and includes the capability for restudy and **lung** lavage when time course or chronic treatments are being considered.

L9 ANSWER 8 OF 17 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001257717 MEDLINE
DOCUMENT NUMBER: 21214768 PubMed ID: 11313798
TITLE: Pulmonary cytokine responses associated with PEI-DNA **aerosol** gene therapy.
AUTHOR: Gautam A; Densmore C L; Waldrep J C
CORPORATE SOURCE: Department of Molecular Physiology and Biophysics, Baylor College of Medicine, 1 Baylor Plaza, Houston, TX 77030, USA.
SOURCE: GENE THERAPY, (2001 Feb) 8 (3) 254-7.
Journal code: 9421525. ISSN: 0969-7128.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010521
Last Updated on STN: 20010521
Entered Medline: 20010517

AB Pulmonary gene therapy with nonviral vectors delivered by instillation or intravenously has typically been associated with co-induction of cytokine responses attributed to the CpG motifs in the bacterial plasmid. Alternative **delivery** systems are being developed to circumvent the cytokine responses to the plasmid. **Aerosol delivery** of polyethylenimine--DNA (PEI-DNA) complexes leads to localized, high levels of transgene expression in the **lungs**. In this study, we show that PEI-DNA **aerosol delivery** is also associated with induction of tumor necrosis factor alpha (TNF-alpha) and interleukin 1 beta (IL-1 beta) in the **lung** and bronchoalveolar lavage fluid (BALF). However, there is no increase in the serum levels of these **cytokines**. The levels of these **cytokines** peak at 5--8 h after **aerosol** exposure for **lung** tissue, and at 24 h for BALF. However, the levels detected are much lower than those observed when PEI-DNA complexes, guanidinium--cholesterol: dioleoylphosphatidyl--ethanolamine liposome--DNA (BGTC:DOPE--DNA) complexes or 1,2-dioleoyl-sn-glycero-3-trimethylammonium--propane--cholesterol:DNA (DOTAP-Chol:DNA) complexes were delivered intravenously. Also, the **lung** cytokine levels were higher when BGTC:DOPE--DNA complexes were delivered by **aerosol** to the mice. Although the mechanism remains to be elucidated, the data suggest that **aerosol** exposure to PEI--DNA complexes can achieve high levels of transgene expression in the **lungs** without inducing high levels of cytokine responses.

L9 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:756484 CAPLUS
DOCUMENT NUMBER: 133:329593
TITLE: Low adenosine anti-sense oligonucleotide, compositions, kit and method for treatment of airway disorders associated with bronchoconstriction, lung inflammation, allergy(ies) and surfactant depletion
INVENTOR(S): Nyce, Jonathan W.
PATENT ASSIGNEE(S): East Carolina University, USA
SOURCE: PCT Int. Appl., 1592 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000062736 | A2 | 20001026 | WO 2000-US8020 | 20000324 |
| WO 2000062736 | A3 | 20011011 | | |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| BR 2000006019 | A | 20010313 | BR 2000-6019 | 20000324 |
| EP 1168919 | A2 | 20020109 | EP 2000-919668 | 20000324 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |

PRIORITY APPLN. INFO.: US 1999-127958P P 19990406
WO 2000-US8020 W 20000324
OTHER SOURCE(S): MARPAT 133:329593

AB An in vivo method of selectively delivering a nucleic acid to a target gene or mRNA, comprises the topical administration, e.g. to the respiratory system, of a subject of a therapeutic amt. of an oligonucleotide (oligo) that is antisense to the initiation codon region, the coding region, the 5' or 3' intron-exon junctions or regions within 2 to 10 nucleotides of the junctions of the gene or antisense to a mRNA complementary to the gene in an amt. effective to reach the target polynucleotide and reducing or inhibiting expression. In addn. a method of treating an adenosine-mediated effect comprises topically administering to a subject an antisense oligo in an amt. effective to treat the respiratory, pulmonary, or airway disease. In order to minimize triggering adenosine receptors by their metab., the administered oligos have a low content of or are essentially free of adenosine. A pharmaceutical compn. and formulations comprise the oligo antisense to an adenosine receptor, genes and mRNAs encoding them, genomic and mRNA flanking regions, intron and exon borders and all regulatory and functionally related segments of the genes and mRNAs encoding the polypeptides, their salts and mixts. Various formulations contain a requisite carrier, and optionally other additives and biol. active agents.

The low-adenosine or adenosine-free (des-A) agent for practicing the method of the invention may be prepd. by selecting a target gene(s), genomic flanking region(s), RNA(s) and/or polypeptide(s) assocd. with a

disease(s) or condition(s) afflicting lung airways, obtaining the sequence of the mRNA(s) corresponding to the target gene(s) and/or genomic flanking region(s), and/or RNAs encoding the target polypeptide(s), selecting at least one segment of the mRNA which may be up to 60 % free of thymidine (T) and synthesizing one or more anti-sense oligonucleotide(s) to the mRNA segments which are free of adenosine (A) by substituting a universal base for A when present in the oligonucleotide. The agent may be prepd. by selection of target nucleic acid sequences with GC running stretches, which have low T content, and by optionally replacing A in the antisense oligonucleotides with a "Universal or alternative base". The agent, compn. and formulations are used for prophylactic, preventive and therapeutic treatment of ailments assocd. with impaired respiration, lung allergy(ies) and/or inflammation and depletion lung surfactant or surfactant hypoprodn., such as pulmonary vasoconstriction, inflammation, allergies, allergic rhinitis, asthma, impeded respiration, lung pain, cystic fibrosis, bronchoconstriction. The present treatment is suitable for administration in combination with other treatments, e.g. before, during and after other treatments, including radiation, chemotherapy, antibody therapy and surgery, among others. Alternatively, the present agent is effectively administered prophylactically or therapeutically by itself for conditions without known therapies or as a substitute for therapies exhibiting undesirable side effects. The treatment of this invention may be administered directly into the respiratory system of a subject so that the agent has direct access to the lungs, or by other effective routes of administration, e.g. topically, transdermally, by implantation, etc., in an amt. effective to reduce or inhibit the symptoms of the ailment.

L9 ANSWER 10 OF 17 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2000392744 MEDLINE
DOCUMENT NUMBER: 20308150 PubMed ID: 10848908
TITLE: Influence of bronchial allergen challenge on histamine release by human basophils.
AUTHOR: Lie W J; Van Der Veen M J; Knol E F; Mul F P; Jansen H M; Roos D; Van Der Zee J S
CORPORATE SOURCE: Central Laboratory of The Netherlands Red Cross Blood Transfusion Service and the Laboratory for Experimental and Clinical and Immunology, Academic Medical Center, University of Amsterdam, The Netherlands.
SOURCE: CLINICAL AND EXPERIMENTAL ALLERGY, (2000 Jun) 30 (6) 882-90.
Journal code: 8906443. ISSN: 0954-7894.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000824
Last Updated on STN: 20000824
Entered Medline: 20000817

AB BACKGROUND: Basophils can be primed by **cytokines** such as interleukin (IL) -3, IL-5 or granulocyte macrophage-colony stimulating factor (GM-CSF). It has been described that the concentrations of these **cytokines** are enhanced at sites of allergic inflammation as well as systemic in allergic asthma. OBJECTIVE: To investigate the priming

status of basophils as detected by thapsigargin-induced histamine release during bronchial allergen challenge. METHODS: Ten subjects allergic to house dust mite were challenged via an **aerosol delivery** system. Spontaneous leucocyte histamine release as well as histamine release induced by various stimuli was measured in vitro at several time points. In addition, **lung** function parameters, serum IL-5 and blood eosinophil counts were evaluated. RESULTS: We found no effect of bronchial allergen challenge upon spontaneous leucocyte histamine release, nor upon histamine release induced by anti-immunoglobulin (Ig) E, house dust mite extract, C5a, fMLP, IL-3, PMA+ thapsigargin or IL-3+ thapsigargin. However, the priming status of basophils as measured by thapsigargin-induced histamine release was enhanced at 24 h after bronchial allergen challenge. Analysis of the individual data showed a heterogeneous initial response (30 min, 6 h) followed by a predominant increase at 24 h after allergen challenge. This increase in the thapsigargin-induced histamine release correlated with the increase in serum IL-5 levels at 24 h after allergen challenge. CONCLUSION: The priming status of human basophils as measured by thapsigargin-induced histamine release is enhanced 24 h after allergen challenge.

L9 ANSWER 11 OF 17 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999394500 MEDLINE
DOCUMENT NUMBER: 99394500 PubMed ID: 10466624
TITLE: Systemic and local interferon gamma gene delivery to the lungs for treatment of allergen-induced airway hyperresponsiveness in mice.
AUTHOR: Dow S W; Schwarze J; Heath T D; Potter T A; Gelfand E W
CORPORATE SOURCE: Department of Medicine, National Jewish Medical and Research Center, Denver, CO 80206, USA.
CONTRACT NUMBER: AI-37905 (NIAID)
HL-36577 (NHLBI)
SOURCE: HUMAN GENE THERAPY, (1999 Aug 10) 10 (12) 1905-14.
Journal code: 9008950. ISSN: 1043-0342.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991207

AB Allergen-induced airway hyperresponsiveness, an animal model of asthma in humans, may respond to immunotherapy with Th1 **cytokines**. For example, local administration of recombinant IL-12 or IFN-gamma, or intratracheal **delivery** of the genes for these **cytokines**, has been shown to reduce the severity of allergen-induced airway hyperresponsiveness (AHR) in rodent models. We reasoned that systemic cytokine gene **delivery** to the **lungs** by intravenous injection of lipid-DNA complexes might also be an effective approach to treatment of allergen-induced AHR. Therefore, the effects of either systemic or local pulmonary IFN-gamma gene **delivery** were evaluated in mice with allergen-induced AHR. The effects of treatment on AHR, airway eosinophilia and cytokine production, and serum IgE concentrations were evaluated in mice that were first sensitized to ovalbumin and then subjected to **aerosol** ovalbumin challenge. Intravenous IFN-gamma gene **delivery** significantly inhibited development of AHR and airway eosinophilia and decreased serum IgE levels, compared with control mice or mice treated with noncoding DNA.

Intratracheal IFN-gamma gene **delivery** also significantly inhibited AHR and airway eosinophilia, but did not affect serum IgE levels. Treatment with recombinant IFN-gamma was much less effective than IFN-gamma gene **delivery** by either route. We conclude that either systemic or local pulmonary **delivery** of a Th1 cytokine gene such as IFN-gamma may be an effective approach for treatment of allergen-induced asthma.

L9 ANSWER 12 OF 17 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 1998099769 MEDLINE
DOCUMENT NUMBER: 98099769 PubMed ID: 9435302
TITLE: IL-6 is an antiinflammatory cytokine required for controlling local or systemic acute inflammatory responses.
AUTHOR: Xing Z; Gauldie J; Cox G; Baumann H; Jordana M; Lei X F; Achong M K
CORPORATE SOURCE: Immunology and Infection Program, Department of Pathology, McMaster University, Hamilton, Ontario, L8N 3Z5 Canada.. xingz@fhs.csu.mcmaster.ca
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (1998 Jan 15) 101 (2) 311-20.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980217
Last Updated on STN: 19980217
Entered Medline: 19980205

AB IL-6 is induced often together with the proinflammatory **cytokines** TNFalpha and IL-1 in many alarm conditions, and circulating IL-6 plays an important role in the induction of acute phase reactions. However, whether this endogenous IL-6 plays any additional pro- or antiinflammatory roles in local or systemic responses remains unclear. In this study, the role of IL-6 in acute inflammatory responses was investigated in animal models of endotoxic **lung** or endotoxemia by using IL-6+/+ and IL-6-/- mice. **Aerosol** exposure of endotoxin induced increased IL-6 and proinflammatory **cytokines** TNFalpha and MIP-2 and a neutrophilic response in the **lung** of IL-6+/+ mice. However, the levels of TNFalpha and MIP-2 and neutrophilia were significantly higher in the **lung** of IL-6-/- mice. The rate of neutrophil apoptosis in these mice was similar to that in IL-6+/+ mice. A low constitutive level of antiinflammatory cytokine IL-10 was not enhanced by endotoxin and remained similar in the **lung** in both IL-6+/+ and IL-6-/- mice. Systemically, intraperitoneal **delivery** of endotoxin resulted in much more pronounced circulating levels of TNFalpha, MIP-2, GM-CSF, and IFNgamma in IL-6-/- mice than in IL-6+/+ mice, and administration of recombinant IL-6 to IL-6-/- mice abolished these differences. In contrast, circulating IL-10 levels were induced to a similar degree in both IL-6+/+ and IL-6-/- mice. Thus, our studies reveal that endogenous IL-6 plays a crucial antiinflammatory role in both local and systemic acute inflammatory responses by controlling the level of proinflammatory, but not antiinflammatory, **cytokines**, and that these antiinflammatory activities by IL-6 cannot be compensated for by IL-10 or other IL-6 family

members.

L9 ANSWER 13 OF 17 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 1998382063 MEDLINE
DOCUMENT NUMBER: 98382063 PubMed ID: 9717963
TITLE: Compartmentalized transgene expression of granulocyte-macrophage colony-stimulating factor (GM-CSF) in mouse lung enhances allergic airways inflammation.
AUTHOR: Lei X F; Ohkawara Y; Stampfli M R; Gauldie J; Croitoru K; Jordana M; Xing Z
CORPORATE SOURCE: Department of Pathology, McMaster University, Hamilton, Ontario, Canada.
SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1998 Aug) 113 (2) 157-65.
Journal code: 0057202. ISSN: 0009-9104.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980917
Last Updated on STN: 19980917
Entered Medline: 19980909

AB To investigate the role of GM-CSF in asthmatic airways inflammation, we have targeted GM-CSF transgene to the airway cells in a mouse model of ovalbumin (OVA)-induced allergic airways inflammation, a model in which there is marked induction of endogenous IL-5 and IL-4 but not GM-CSF. Following intranasal **delivery** of a replication-deficient adenoviral gene transfer vector (Ad), transgene expression was found localized primarily to the respiratory epithelial cells. Intranasal **delivery** of 0.03 x 10(9) plaque-forming units (PFU) of AdGM-CSF into naive BALB/c mice resulted in prolonged and compartmentalized release of GM-CSF transgene protein with a peak concentration of approximately 80 pg/ml detected in bronchoalveolar lavage fluid (BALF) at day 7, but little in serum. These levels of local GM-CSF expression per se resulted in no eosinophilia and only a minimum of tissue inflammatory responses in the **lung** of naive mice, similar to those induced by the control vector. However, such GM-CSF expression in the airways of OVA-sensitized mice resulted in a much greater and sustained accumulation of various inflammatory cell types, most noticeably eosinophils, both in BALF and airway tissues for 15-21 days post-OVA **aerosol** challenge, at which times airways inflammation had largely resolved in control mice. While the levels of IL-5 and IL-4 in BALF and the rate of eosinophil apoptosis were found similar between different treatments, there was an increased number of proliferative leucocytes in the **lung** receiving GM-CSF gene transfer. Our results thus provide direct experimental evidence that GM-CSF can significantly contribute to the development of allergic airways inflammation through potentiating and prolonging inflammatory infiltration induced by **cytokines** such as IL-5 and IL-4.

L9 ANSWER 14 OF 17 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 1998112872 MEDLINE
DOCUMENT NUMBER: 98112872 PubMed ID: 9451042
TITLE: **Aerosol** cyclosporine prevents acute allograft rejection in experimental lung transplantation.
AUTHOR: Mitruka S N; Pham S M; Zeevi A; Li S; Cai J; Burckart G J; Yousem S A; Keenan R J; Griffith B P

CORPORATE SOURCE: Department of Cardiothoracic Surgery, University of Pittsburgh School of Medicine, PA 15261, USA.
CONTRACT NUMBER: RO1-HL48091-03 (NHLBI)
SOURCE: JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY, (1998 Jan) 115 (1) 28-36; discussion 36-7.
Journal code: 0376343. ISSN: 0022-5223.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980226
Last Updated on STN: 19980226
Entered Medline: 19980218

AB BACKGROUND: The incidence of acute rejection and the morbidity of systemic cyclosporine (INN: cyclosporine) after **lung** transplantation is significant. Experimental evidence suggests that the allograft locally modulates the immune mechanisms of acute rejection. The purpose of this study was to determine whether aerosolized cyclosporine would prevent acute cellular rejection, achieve effective graft concentrations with low systemic drug **delivery**, and locally affect production of the inflammatory **cytokines** involved in acute rejection. METHODS: Unilateral orthotopic left **lung** transplantation was performed in 64 rats (ACI to Lewis), which were divided into eight groups (each group, n = 8): group A, no treatment; groups B to D, **aerosol** cyclosporine 1 to 3 mg/kg per day, respectively; group E to H, systemic cyclosporine 2, 5, 10, and 15 mg/kg per day, respectively. After the animals were killed on postoperative day 2, 4, or 6, the transplanted **lung**, native **lung**, spleen, and blood were collected. Histologic studies, high-pressure liquid chromatography for trough cyclosporine concentrations, and reverse-transcriptase polymerase chain reaction for cytokine gene expression were performed. RESULTS: Untreated animals showed grade 4 rejection by postoperative day 6. **Aerosol** cyclosporine prevented acute rejection in a dose-dependent fashion, with group D animals (3 mg/kg per day) showing minimal grade 1 changes. Among animals receiving systemic cyclosporine, only group H (15 mg/kg per day) controlled (grade 1) rejection. However, **aerosol** cyclosporine, at an 80% lower dose, achieved significantly lower concentrations of cyclosporine in the graft (12,349 vs 28,714 ng/mg, p = 0.002004) and blood (725 vs 3306 ng/ml, p = 0.000378). Group F (systemic 5 mg/kg per day) had higher cyclosporine concentrations in the blood than group D (p = 0.004572) and similar tissue concentrations (p = 0.115180), yet had grade 2 rejection. Reverse-transcriptase polymerase chain reaction demonstrated equivalent suppression of inducible nitric oxide synthase but a 20- to 25-fold higher expression of interleukin-6, interleukin-10, and interferon-gamma in group D versus group H recipient allografts. CONCLUSION: Local **delivery** of cyclosporine by **aerosol** inhalation dose-dependently prevented acute pulmonary allograft rejection. Effective graft levels and low systemic drug **delivery** required significantly lower doses than systemic therapy alone. The gene expression of proinflammatory **cytokines** involved in allograft rejection was suppressed by **aerosol** cyclosporine therapy.

L9 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:132147 CAPLUS
DOCUMENT NUMBER: 118:132147

TITLE: **Aerosols** for delivery of proteins
INVENTOR(S): Lohmann, Helmut; Pollmann, Wolfgang; Schnecker, Kurt; Zierenberg, Bernd
PATENT ASSIGNEE(S): Boehringer Ingelheim KG, Germany
SOURCE: Ger. Offen., 3 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 4117078 | A1 | 19921126 | DE 1991-4117078 | 19910525 |
| WO 9221332 | A1 | 19921210 | WO 1992-EP1080 | 19920516 |
| W: AT, AU, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KR, LU, NL, NO, PL, RO, RU, SE, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| AU 9217557 | A1 | 19930108 | AU 1992-17557 | 19920516 |

PRIORITY APPLN. INFO.: DE 1991-4117078 19910525
WO 1992-EP1080 19920516

AB From aq.-formulations therapeutic proteins, **aerosols** (for delivery to lung) are produced by ultrasound atomization. The prepns. could contain addnl. excipients such as surfactants, emulsifiers, stabilizers and preservatives. An ultrasound atomizer with a frequency of 2-3 MHz is used.

L9 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:443473 CAPLUS
DOCUMENT NUMBER: 109:43473
TITLE: Device and dispersion for intrapulmonary delivery of polypeptide growth factors and cytokines
INVENTOR(S): Daugherty, Ann Leslie
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 257956 | A2 | 19880302 | EP 1987-307276 | 19870818 |
| EP 257956 | A3 | 19890419 | | |
| EP 257956 | B1 | 19920520 | | |
| EP 257956 | B2 | 20001122 | | |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| AT 76311 | E | 19920615 | AT 1987-307276 | 19870818 |
| ES 2032831 | T3 | 19930301 | ES 1987-307276 | 19870818 |
| JP 63051868 | A2 | 19880304 | JP 1987-207361 | 19870819 |
| JP 2573959 | B2 | 19970122 | | |
| CA 1292182 | A1 | 19911119 | CA 1987-544836 | 19870819 |
| US 6099517 | A | 20000808 | US 1993-128058 | 19930927 |
| US 6402733 | B1 | 20020611 | US 2000-552199 | 20000419 |

PRIORITY APPLN. INFO.: US 1986-897962 A 19860819
EP 1987-307276 A 19870818
US 1989-312325 B1 19890216
US 1991-762039 B1 19910917

US 1992-982268 B1 19921125
US 1993-128058 A1 19930927

AB Polypeptides selected from growth factors and cytokines are administered by intrapulmonary inhalation: compressed air entrains a soln. of the polypeptide from a reservoir, and the polypeptide soln. is dispersed by a nebulizer and inhaled directly into the lungs via a mouthpiece. Using the invention device, an anesthetized baboon was treated for 30 min with somatrem in a mannitol/phosphate buffer, at 22 cm H2O at a rate of 1.8 mg somatrem/min, allowed to breathe normally for 20 min, and treated again for 30 min. Serum human growth hormone peaked at >280 ng/mL after the second dose, and continued to show elevated levels (>80 ng/mL) after 28 h.

The long term drug delivery is surprising, as it is generally believed that drug deliver of >12 h is not achievable by intrapulmonary inhalation.

L9 ANSWER 17 OF 17 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 88198993 MEDLINE
DOCUMENT NUMBER: 88198993 PubMed ID: 3283235
TITLE: **Lung**-specific **delivery** of **cytokines** induces sustained pulmonary and systemic immunomodulation in rats.
AUTHOR: Debs R J; Fuchs H J; Philip R; Montgomery A B; Brunette E N; Liggitt D; Patton J S; Shellito J E
CORPORATE SOURCE: Cancer Research Institute, University of California, San Francisco 94143.
SOURCE: JOURNAL OF IMMUNOLOGY, (1988 May 15) 140 (10) 3482-8. Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198806
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19880609

AB The recombinant cytokines IFN-gamma and TNF-alpha stimulate several macrophage-mediated functions important in host defense. However, systemic administration of cytokines may be limited by significant host toxicity. We investigated whether aerosolized cytokines can stimulate alveolar macrophage and blood monocyte function, and whether they induce an inflammatory response in the lungs of normal rats. We found that aerosolized murine rIFN-gamma or recombinant human TNF-alpha increased IL-1 production by both alveolar macrophages and blood monocytes for at least 5 days after administration. Furthermore, murine rIFN-gamma increased the expression of Ia Ag on alveolar macrophages and human rTNF-alpha increased alveolar macrophage- and blood monocyte-mediated tumor lysis. Sequential aerosolization of IFN-gamma and TNF-alpha significantly increased both IL-1 release and Ia expression compared to either cytokine administered alone. Aerosolized human rTNF-alpha achieved lung levels comparable to those produced by an i.v. TNF-alpha dose reported to cause diffuse organ injury and death in rats. However, plasma TNF-alpha levels were several thousand-fold lower after **aerosol** administration. Aerosolized cytokines did not induce lung edema or an inflammatory cell infiltrate within the airways or alveoli. Aerosolized human rTNF-alpha alone, or murine rIFN-gamma and human rTNF-alpha, induced margination of leukocytes in pulmonary blood vessels 1 day after

aerosolization, and a few small foci of pulmonary hemorrhage 5 days later.

We conclude that **aerosol** administration of IFN-gamma or TNF-alpha enhances both pulmonary and systemic monocyte function, and that the combination of IFN-gamma and TNF-alpha produce additive or synergistic effects. Aerosolized cytokines induce only a minimal pulmonary inflammatory response. Aerosolized TNF-alpha produces high cytokine levels in the lung but very low uptake into the circulation.

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| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 68.42 | 68.63 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | -8.46 | -8.46 |

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YOU HAVE REQUESTED DATA FROM 79 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 79 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:805245 CAPLUS
DOCUMENT NUMBER: 137:277763
TITLE: Myeloid blood CD11c+ dendritic cells and monocyte-derived dendritic cells differ in their ability to stimulate T lymphocytes
AUTHOR(S): Osugi, Yuko; Vuckovic, Slavica; Hart, Derek N. J.
CORPORATE SOURCE: Department of Developmental Medicine (Pediatrics), D-5, Osaka University Graduate School of Medicine, Japan
SOURCE: Blood (2002), 100(8), 2858-2866
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Dendritic cells (DCs) initiate and direct immune responses. Recent studies have defined different DC populations, therefore we undertook this study comparing 2 types of myeloid DCs: blood CD11c+ DCs and in vitro monocyte-derived DCs (Mo-DCs), which are both candidates as cellular adjuvants for cancer immunotherapy. Blood CD11c+ DCs were prepd. by cell sorting from peripheral blood mononuclear cells cultured overnight in RPMI 1640 medium supplemented with autologous or pooled AB serum. Mo-DCs were prepd. in the same medium using granulocyte macrophage-colony-stimulating factor (GM-CSF)/interleukin 4 (IL-4) and differentiated/activated with lipopolysaccharide or monocyte-conditioned medium (ActMo-DCs). Morphol., differences between the DC prepns. were noted both at a light and electron microscopic level. Blood CD11c+ DCs expressed similar levels of HLA-DR, CD40, CD86, and CD83 as Mo-DCs. CD209 was present on Mo-DCs but not on blood CD11c+ DCs. Blood CD11c+ DCs generated a lower proliferative mixed leukocyte response (MLR) than Mo-DCs. Blood CD11c+ DCs loaded with 0.1 .mu.g/mL tetanus toxoid (TT)-generated greater T lymphocyte proliferative responses than did Mo-DCs or ActMo-DCs, but when loaded with higher TT concns. no difference in T lymphocyte proliferative response was obsd. Keyhole limpet hemocyanin (KLH)-loaded blood CD11c+ DCs generated greater T lymphocyte proliferative responses than Mo-DCs or ActMo-DCs. Allogeneic MLR- or KLH-specific responses induced by blood CD11c+ DCs generated more Th1 effectors than the responses induced by Mo-DCs or ActMo-DCs. These data establish several differences in the properties of blood CD11c+ DCs, Mo-DCs, and ActMo-DCs, which suggest that blood DCs merit further consideration as DC prepns. for clin. programs are evolved.
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 79 MEDLINE
DUPLICATE 1
ACCESSION NUMBER: 2002357112 MEDLINE
DOCUMENT NUMBER: 22095350 PubMed ID: 12100724
TITLE: Regulation of HLA-DR and co-stimulatory molecule expression on natural killer T cells by granulocyte-macrophage colony-stimulating factor.
AUTHOR: Saikh Kamal U; Kissner Teri; Ulrich Robert G
CORPORATE SOURCE: Laboratory of Molecular Immunology, Army Medical Research Institute of Infectious Diseases, Frederick, MD 21702-5011, USA.
SOURCE: IMMUNOLOGY, (2002 Jul) 106 (3) 363-72.
Journal code: 0374672. ISSN: 0019-2805.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020709
Last Updated on STN: 20020829
Entered Medline: 20020828
AB A subset of mononuclear cells present in most tissues coexpresses receptors of both natural killer (NK) and T cells. Although linked to antiviral immunity, the function of these putative NKT cells is uncertain. We present evidence that human CD56+ DR- NKT cells exhibit hybrid adaptive and innate immune functions. These cells spontaneously lysed tumour cell targets and upon engagement of T-cell antigen receptors secreted the cytokines interferon-gamma and granulocyte-macrophage colony-stimulating factor (GM-CSF). Conversely, GM-CSF treatment transformed the NKT cells into dendritic cells, inducing rapid expression of HLA-DR and the co-stimulatory molecules CD80 and CD86. The ability to stimulate tetanus toxoid-specific responses from naive T cells was acquired within 3 days of activating CD56+ NKT cells with GM-CSF. These results suggest a potential role for NKT cells in the initiation and control of primary immunity during the acute phase of infection.

L4 ANSWER 3 OF 79 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:261703 BIOSIS
DOCUMENT NUMBER: PREV200200261703
TITLE: Flt3 ligand safely increases dendritic cells after autologous transplantation which may be useful to correct the impaired immune response to neo-antigens after autologous transplant.
AUTHOR(S): Miller, Jeffrey S. (1); Weisdorf, Daniel J. (1); Panoskaltsis-Mortari, Angela (1); Curtsinger, Julie R. (1); Blazar, Bruce R. (1)
CORPORATE SOURCE: (1) Blood and Marrow Transplant Program, University of Minnesota, Minneapolis, MN USA
SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 860a. http://www.bloodjournal.org/. print. Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001 ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Relapse is still the most common cause of treatment failure after autologous transplant and cancer vaccines may eradicate minimal residual disease. However, even the best vaccine strategy will fail if the immune system is not able to respond appropriately. To test immune integrity, we vaccinated 15 normal volunteers with 1 mg of KLH, a neo-antigen that humans would not have been exposed to previously and 10 received tetanus toxoid (TT), an antigen that all subjects have seen. Proliferation assays were performed in limiting dilutions to allow frequency calculations. The frequency of KLH-specific mononuclear cells increased 20-fold 28 days after a KLH vaccine and 100% of normal subjects responded. As expected, the frequency of TT-specific cells was higher at baseline and increased 3.6-fold after vaccination. Similar responses were seen using ELISPOT readouts for cells producing INF-GAMMA. KLH elicited potent IgM, IgG1, IgG2 and IgG3 specific antibody responses in all normal subjects and TT-specific IgG1 increased as well. We next vaccinated 6 patients (myeloma, CML, breast cancer) 3-19 months after autologous transplant. In marked contrast to normal subjects, only 1 of 6 patients exhibited a KLH proliferative response and 1 of 5 exhibited a TT response. No patient mounted a specific humoral response. The poor response in transplant patients is of major concern if vaccines are to be added early when disease burden is lowest. Since immune integrity is diminished after autologous transplant, we explored the role of outpatient administration of flt3 ligand given as a subcutaneous injection (20 mug/kg) QOD for a total of 21 doses in a phase I clinical trial. Patients were eligible for this study 56-112 days after autologous transplant if they had hematologic recovery and no ongoing therapy related toxicities. Eight patients have started Flt3L on this trial and five have completed therapy. The first cohort of 5 patients did not receive KLH. There has been no constitutional symptoms related to this immunotherapy and no clinical toxicity or hospitalizations. Monocytes were increased in all patients on therapy. Dendritic cell (DC) numbers determined by 4-color immunophenotype analysis from blood at day 14 showed a median 25-fold (4-52-fold) increase in CD11c+, HLA-DR+, CD14-DC compared to blood obtained prior to initiating therapy. Co-stimulatory molecule expression (CD80 and CD86) on in vivo mobilized DC was lower than that found on monocyte derived DC generated in vitro. Two of three evaluable patients had an increased ability to stimulate an allogeneic mixed lymphocyte reaction on day 14 of therapy and the third patient was unchanged compared to baseline. There was no significant change in NK cell numbers or cytotoxicity assays against K562 targets throughout the study period suggesting that NK cells are not stimulated in vivo by flt3 ligand as found in the mouse. The next 5 patients on study will receive KLH to determine whether flt3 ligand can serve as a vaccine adjuvant to illicit a neo-antigen immune response after autologous transplantation. We conclude that flt3 ligand can be administered safely early after autologous transplant to increase circulating DCs which may be useful alone or in combination with other agents to elicit specific anti-tumor immunity.

L4 ANSWER 4 OF 79 MEDLINE
DUPLICATE 2
ACCESSION NUMBER: 2001161157 MEDLINE
DOCUMENT NUMBER: 21159443 PubMed ID: 11260079
TITLE: Recognition of chronic myelogenous leukaemia cells by autologous T lymphocytes primed in vitro against the patient's dendritic cells.
AUTHOR: Muller L; Provenzani C; Faul C; Pawelec G
CORPORATE SOURCE: Tubingen Ageing and Tumour Immunology Group (TATI), Section

for Transplantation Immunology, University of Tubingen,
Otfried-Muller Str. 10, D-72076 Tubingen, Germany..
ludmilla.mueller@med.uni-tuebingen.de
SOURCE: BRITISH JOURNAL OF HAEMATOLOGY, (2001 Mar) 112 (3) 740-8.
Journal code: 0372544. ISSN: 0007-1048.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010417
Last Updated on STN: 20010417
Entered Medline: 20010412
AB Defects in immune responses are common in patients with chronic
myelogenous leukaemia (CML). However, using dendritic cells (DCs) to
promote T-cell immunity in vitro may nonetheless elicit potent specific
anti-tumour responses for use in immunotherapy. Here, we show that DCs
generated from CML patients had a typical dendritic phenotype and were
able to stimulate autologous T cells. Three primed T-cell lines
were studied in more detail in one patient. They were stimulated by
autologous CML cells, but not by normal non-leukaemic cells from the
patient's HLA-identical sibling. This was blocked by HLA-
DR-specific, but not HLA-DQ- or HLA-DP-specific antibodies.
CML-stimulated cytokine secretion, including interferon-
gamma and granulocyte macrophage-colony stimulating factor,
suggested a Th1-type phenotype for these sensitized anti-leukaemic T
cells. This study therefore shows that cells with a functional dendritic
phenotype can be generated from the blood of CML patients and are potent
inducers of T-cell responses to tumour cells. This approach allows
sensitization of patients' T cells by their own particular tumour without
the need to identify the exact leukaemia antigens involved, and may find
application in immunotherapy of CML.

L4 ANSWER 5 OF 79 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:186773 BIOSIS
DOCUMENT NUMBER: PREV200200186773
TITLE: Feasibility of immunotherapy using donor CD8+ T cells
stimulated with leukemic cell- or donor CD14+ cell derived
dendritic cells (DC) against leukemia relapsing after
hematopoietic stem cell transplantation (HSCT.
AUTHOR(S): Lee, Je-Jung (1); Chung, Ik-Joo (1); Kook, Hoon (1); Hwang,
Tai-Ju (1); Nam, Chan-Eun (1); Nam, Jong-Hee; Lee,
Hyun-Cheol; Takaue, Yoichi; Kim, Hyeoung-Joon (1)
CORPORATE SOURCE: (1) Blood and Marrow Transplant Program, Chonnam National
University Medical School, Gwangju South Korea
SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp.
388a. http://www.bloodjournal.org/. print.
Meeting Info.: 43rd Annual Meeting of the American Society
of Hematology, Part 1 Orlando, Florida, USA December 07-11,
2001
ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
AB In relapsing leukemia after allogeneic HSCT, donor lymphocyte infusions
(DLI) have been used as a salvage therapy based on the
graft-versus-leukemia effect mediated by T-cell effectors. Though
effective in the chronic phase of CML, the potential of DLI has been
limited in patients with AML, ALL, or MDS. DLI is further complicated by
the induction of acute graft-versus-host disease (GVHD) or bone marrow
aplasia. To overcome these problems, a possible alternative approach
includes the application of selected immune effector cells. In addition to
difficulty to generate them, however, leukemic cell-derived DC
(leukemic-DC) have been hampered by the inadequate potency of T-cell
stimulation due to the lower expression of molecules related to adhesion,
MHC, and the costimulatory pathway compared to normal DC. For leukemia
relapsing after allogeneic HSCT, we investigated the possibility of
immunotherapy using target-specific donor CD8+ T cells, which were
generated by leukemic-DC or donor CD14+ cell-derived DC (donor-DC) pulsed
with leukemic cell lysates. To generate leukemic-DC, mononuclear cells
isolated from leukemic patients who relapsed after transplantation were
cultured in medium with GM-CSF (100 ng/mL), IL-4 (100 ng/mL), and
TNF-alpha (50 ng/mL) for 8-10 days. Simultaneously, CD14+ cells were
isolated from HLA-matched donors using Mini-MACS, and cultured with GM-CSF
(50 ng/mL) and IL-4 (50 ng/mL). Maturation of donor-DC was induced by the
addition of TNF-alpha on day 6 and the DC were harvested on day 9. For
evaluation of leukemic-DC and donor-DC, morphologic studies using
May-Grunwald-Giemsa staining, phenotypic studies using several mouse
monoclonal antibodies, allogeneic mixed lymphocyte reaction for normal

donor CD3+ T cells using 3(H)-methylthymidine, and FISH analysis were
performed. For cytotoxic assay, CD8+ T cells isolated from a transplant
donor using Mini-MACS were stimulated on days 0 and 10 by leukemic-DC or
donor-DC which were pulsed with leukemic cell lysates, and further
cocultured with leukemic cells to perform LDH assay or IFN-gamma ELISA on
day 20. We observed that cells from both groups showed similar typical
features of mature DC. The leukemic-DC were derived from original leukemic
cells, as shown by -7 or bcr/abl rearrangement using FISH analysis.
Although leukemic-DC highly expressed HLA-DR and CD54,
the expression of CD80, CD83, CD86, CD1a, and CD40 on leukemic-DC was
significantly lower compared to donor-DC. Donor-DC had a higher capacity
to stimulate allogeneic CD3+ T cells compared to leukemic-DC.
Donor CD8+ T cells stimulated by leukemic-DC or donor-DC have more potent
cytotoxic activity than unprimed CD8+ T cells, while a slightly higher
cytotoxicity was observed in donor-DC compared to leukemic-DC. These
results suggest that donor CD8+ T cells stimulated with leukemic-DC or
donor-DC be feasible as an alternative immunotherapy to DLI for the
application to leukemic patients who relapse after allogeneic HSCT,
although further studies are needed to investigate the clinical efficacy
and the potential risk of GVHD associated with this strategy.

L4 ANSWER 6 OF 79 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
ACCESSION NUMBER: 2000:486589 BIOSIS
DOCUMENT NUMBER: PREV200000486589
TITLE: Role and expression of CD4O on human retinal pigment
epitlielial cells.
AUTHOR(S): Willermain, Francois (1); Caspers-Velu, Laure; Baudson,
Nathalie; Dubois, Christine; Hamdane, Malika; Willems,
Fabienne; Velu, Thierry; Bruyns, Catherine
CORPORATE SOURCE: (1) ULB, Cmpus Erasme, I.R.I.B.H.N., Route de Lennik 808,
Building C, 6th Floor, Room C6 117, Bruxelles Belgium
SOURCE: IOVS, (OCTOBER, 2000) Vol. 41, No. 11, pp. 3485-3491.
print.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Purpose: To examine the CD40 costimulatory molecule expression on normal
resting or activated adult human retinal pigment epithelium (hRPE) cells
and to evaluate its role as an activation molecule considering the
potential antigen presentation functions of hRPE cells. Methods:
Expression of HLA-DR and costimulatory (CD40, B7.1,
B7.2, CD54, and CD58) molecules on hRPE cells was analyzed by flow
cytometry. CD40 triggering was performed using soluble CD40L or cocultures
with CD40L transfected fibroblasts. Interleukin (1L)-6, -8, -10, and -12
secretions were measured by enzyme-linked immunosorbent assay. Antigen
presentation function of hRPE cells was assessed by coculturing hRPE cells
with allogeneic T cells. T-cell proliferation was measured by
(3H)-thymidine incorporation, and T-cell apoptosis by measurement of
caspase-3 activity. Results: Interferon (IFN) gamma-activated hRPE cells
expressed CD40 but not B7.1 or B7.2. Although interferon
gamma enhanced IL-6 and IL-8 production, CD40 triggering of IFN
gamma- activated hRPE cells did not induce IL-12 secretion. hRPE cells did
not stimulate allogeneic resting T cells and downregulated
phytohemagglutlnin-activated allogeneic T cells via a cell-to-cell
contact-dependent mechanism. Some induction of apoptosis was detected.
Conclusions: CD40 is expressed on IFN gamma-activated hRPE cells. Its
ligation leads to an increased production of IL-6 and IL-8 but fails to
induce B7.1 or B7.2 expression, or to induce IL-12 secretion. Accordingly,
hRPE cells do not activate allogenic T cells but inhibit T-cell
proliferation, partly through induction of apoptosis. These results
suggest that hRPE cells could be implicated more in a deviant antigen
presentation. If the exact molecular mechanisms are unclear, it is likely
that CD40-CD40L interaction could play a role in this process.

L4 ANSWER 7 OF 79 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2002047725 MEDLINE
DOCUMENT NUMBER: 21632502 PubMed ID: 11776063
TITLE: Effect of immunoglobulin G from patients with Graves'
ophthalmopathy and interferon gamma in
intercellular adhesion molecule-1 and human leucocyte
antigen-DR expression in human retroocular fibroblasts.
AUTHOR: Li Y; Chen L; Teng W; Shan Z; Li Z
CORPORATE SOURCE: Department of Endocrinology, First Clinical College, China
Medical University, Shenyang 110001, China.
SOURCE: CHINESE MEDICAL JOURNAL, (2000 Aug) 113 (8) 752-5.
Journal code: 7513795. ISSN: 0366-6999.
PUB. COUNTRY: China

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020202
Entered Medline: 20020201
AB OBJECTIVE: To detect the expression of intercellular adhesion molecule-1
(ICAM-1) and human leucocyte antigen-DR (HLA-DR) on
retroocular fibroblasts (RFs) by immunoglobulin G (IgG) from patients with
Graves' ophthalmopathy (GO) and interferon gamma
(IFN-gamma) and to study the possible mechanism of humoral immunity and
cellular immunity in the pathogenesis of GO. METHODS: Purified IgG was
obtained from 23 patients (GO 10, Graves' disease 9, toxic multinodular
goiter 4) and 8 normal persons. Cytokine IFN-gamma and thyroid stimulating
hormone (TSH) were incubated with normal human RF cultured in vitro.
Antigen expression on RFs induced by stimulators was examined using
immunofluoresence staining and a flow cytometer. RESULTS: RFs
spontaneously expressed ICAM-1, but did not express HLA-
DR. All IgGs from patients with GO and other thyroid diseases as
well as from normal persons could not stimulate the expression
of ICAM-1 on RFs. IFN-gamma and TSH significantly enhanced the expression
of ICAM-1 in dose-dependent manner ($P < 0.05$). Only IFN-gamma could
stimulate RFs to express HLA-DR ($P < 0.05$).
CONCLUSIONS: IgG from patients with GO did not stimulate the
expression of ICAM-1 and HLA-DR on the surface of
cultured normal human RFs. IFN-gamma was the important factor for
intiating and promoting autoimmune reactions in GO. We need to pay more
attention to TSH, as it may possibly play a promoting role in the
pathogenesis in GO.

L4 ANSWER 8 OF 79 MEDLINE
DUPLICATE 5
ACCESSION NUMBER: 2000117955 MEDLINE
DOCUMENT NUMBER: 20117955 PubMed ID: 10652024
TITLE: Accessory role of human peritoneal mesothelial cells in
antigen presentation and T-cell growth.
AUTHOR: Hausmann M J; Rogachev B; Weiler M; Chaimovitz C;
Douvdevani A
CORPORATE SOURCE: Department of Nephrology, Soroka Medical Center, Ben-Gurion
University of the Negev, Faculty of Health Sciences,
Beer-Sheva, Israel.
SOURCE: KIDNEY INTERNATIONAL, (2000 Feb) 57 (2) 476-86.
Journal code: 0323470. ISSN: 0085-2538.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000320
Last Updated on STN: 20000320
Entered Medline: 20000309
AB BACKGROUND: To assess the role of human peritoneal mesothelial cells
(HPMCs) in the generation of an immune response during peritonitis, we
tested their ability to activate T-cells by antigen presentation (AP) and
by the secretion of interleukin-15 (IL-15). IL-15 is a potent leukocyte
activator that stimulates the proliferation of CD4+, CD8+, and B
and natural killer (NK) cells. METHODS: HPMCs and mononuclear cells were
derived from six volunteer patients who underwent elective abdominal
surgery. Flow cytometry was used to analyze human lymphocyte antigen-DR (
HLA-DR), intercellular adhesion molecule-1 (ICAM-1), and
B7 molecules on HPMCs. Affinity-purified CD4 cells were used for AP
assays. We used a specific enzyme-linked immunosorbent assay to detect
interferon-gamma (IFN-gamma), IL-2, and IL-15 protein
and reverse transcription-polymerase chain reaction for mRNA analysis.
RESULTS: HPMCs expressed HLA-DR molecules following
IFN-gamma treatment. ICAM-1 molecules were expressed at high levels, and
B7-1 and B7-2 molecules could not be detected. The accessory function of
HPMCs was assayed by T-cell stimulation using anti-CD3 antibodies (OKT3).
HPMCs were essential for a significant OKT3-induced T-cell proliferation.
Anti-ICAM-1 antibodies blocked OKT3-induced proliferation. HPMCs served as
effective antigen-presenting cells when Tetanus toxoid (TT) or
Staphylococcus aureus-alpha-toxin were used as antigens. IFN-gamma, IL-2,
and IL-15 accumulated during AP reactions. We found that IL-15 is produced
by HPMCs, and IFN-gamma up-regulated its mRNA levels and protein secretion
in a dose-dependent manner. We also detected IL-15 in the peritoneal
effluent of patients undergoing continuous peritoneal dialysis treatment.
In patients suffering from peritonitis, IL-15 levels were elevated (35.0
+/- 6.0 pg/mL, N = 10) as compared with noninfected patients (16.2 +/- 4.0
pg/mL, N = 7). CONCLUSIONS: HPMCs participate in the peritoneal immune
response against invading pathogens by AP. For this process, ICAM-1 is the
major accessory molecule. In addition, HPMCs may contribute to T-cell

activation by secretion of IL-15.

L4 ANSWER 9 OF 79 MEDLINE
DUPLICATE 6
ACCESSION NUMBER: 2000241576 MEDLINE
DOCUMENT NUMBER: 20241576 PubMed ID: 10780664
TITLE: CD4+ T cell-mediated cytotoxicity toward thyrocytes: the
importance of Fas/Fas ligand interaction inducing apoptosis
of thyrocytes and the inhibitory effect of thyroid-stimulating hormone.
AUTHOR: Kawakami A; Matsuoka N; Tsuboi M; Koji T; Urayama S; Sera
N; Hida A; Usa T; Kimura H; Yokoyama N; Nakashima T;
Ishikawa N; Ito K; Kawabe Y; Eguchi K
CORPORATE SOURCE: The First Department of Internal Medicine, Nagasaki
University School of Medicine, Tokyo, Japan.
SOURCE: LABORATORY INVESTIGATION, (2000 Apr) 80 (4) 471-84.
Journal code: 0376617. ISSN: 0023-6837.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000518
Last Updated on STN: 20000518
Entered Medline: 20000509
AB The accumulation of activated CD4+ T cells and antigen (Ag)-dependent
cellular interactions between thyrocytes and CD4+ T cells have been
determined in thyroid gland from patients with Graves' disease. The
Fas/Fas ligand (FasL) interaction between antigen-presenting cells and T
cells regulates the apoptosis of the former cells triggered by the latter
cells. The inhibition of Fas-mediated apoptosis in thyrocytes could be a
underlying mechanism of hyperplasia of thyrocytes in patients with Graves'
disease. We investigated the potential role of Fas/FasL interaction
between thyrocytes and CD4+ T cells in the induction of Fas-mediated
apoptosis of the former cells induced by the latter cells. The presence of
only a few specific T cells responsive to a putative autoantigen has
hampered the investigation of specific T cell activation toward
antigen-presenting cells (APCs). Therefore, we used a superantigen,
staphylococcal enterotoxin B (SEB), to examine specific T cell activation
toward thyrocytes in vitro since it stimulates a large
proportion of T cells with particular Vbeta elements. Spontaneous
apoptosis of thyrocytes in culture was not found even in the presence of
various kinds of cytokines. In contrast, a clear induction of Fas-mediated
apoptosis by anti-Fas IgM was determined in interferon-
gamma (IFN-gamma)-stimulated thyrocytes. In addition, a
significant cytotoxicity of purified CD4+ T cells toward
IFN-gamma-stimulated thyrocytes in the presence of SEB was induced, and
the addition of anti-HLA-DR and -DQ monoclonal
antibodies (mAbs) or blockade of the Fas/FasL interaction reduced this
cytotoxicity. FasL expression of CD4+ T cells cocultured with
IFN-gamma-stimulated thyrocytes in the presence of SEB was clearly
induced. Furthermore, the addition of mAbs against CD54 and CD58 inhibited
both cytotoxicity and FasL expression of CD4+ T cells. The cytotoxicity of
CD4+ T cells toward IFN-gamma-stimulated, SEB-pulsed thyrocytes was
markedly inhibited when we used thyrocytes cultured with IFN-gamma in the
presence of thyroid-stimulating hormone (TSH) as target cells. Our results
suggest that 1) CD4+ T cells were activated by thyrocytes expressing MHC
class II molecules in an SEB-dependent manner and then expressed FasL. 2)
These activated FasL+ CD4+ T cells killed thyrocytes by interacting with
Fas on thyrocytes and FasL on activated CD4+ T cells. The presence of
costimulating molecules such as CD54 and CD58 on thyrocytes was also
necessary to generate activated FasL+ CD4+ T cells. 3) Since the actions
of thyroid stimulating antibody (TSAb) toward thyrocytes are similar to
those of TSH, one goitrogenic activity of TSAb may, in part, be due to the
inhibitory effect on Fas-mediated apoptosis of thyrocytes triggered by
activated CD4+ T cells.

L4 ANSWER 10 OF 79 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:314818 BIOSIS
DOCUMENT NUMBER: PREV200100314818
TITLE: In vitro primining of normal donor PBMC with myeloma
protein pulsed dendritic cells.
AUTHOR(S): Kim, S. B. (1); Baskar, S.; Kwak, L. W.
CORPORATE SOURCE: (1) Department of Medicine, Asan Medical Center, University
of Ulsan, Seoul South Korea
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 2, pp.
289b. print.
Meeting Info.: 42nd Annual Meeting of the American Society
of Hematology San Francisco, California, USA December
01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Dendritic cells (DC) are very efficient antigen-presenting cells (APC) and have been used to directly present exogenous antigen to CD8+ T cells. In vitro priming of T cells with DC pulsed with weak antigens such as tumor idiotype (Id), is an attractive strategy to generate tumor-specific cytotoxic T lymphocytes (CTL). A previous report from this laboratory demonstrated generation of tumor-specific CTL using autologous DC pulsed with patient Id (Blood, Oct. 15, 2000). In the present study, we extend our investigation to generate antigen-specific T cells from normal donor PBMC by in vitro priming using autologous DC as APC. After 2hr of incubation of PBMC, adherent cells were cultured for generation of DC with IL-4 and GM-CSF, and DC were harvested on different days. Phenotypic analysis showed that DC obtained at day 8, day 10, and day 12 expressed high levels of HLA-DR. The expression of CD80, CD83 and CD86, however, were higher in DC obtained at day 8 compared to those at day 10 and day 12. We compared the ability of DC to stimulate T cell cytokine responses to keyhole limpet, hemocyanin (KLH), tetanus toxoid (TT), and Id. In vitro primed T cells (2-4 cycles of stimulation with Ag and DC) showed significant cytokine responses (IFNgamma, TNFalpha, GM-CSF, IL-13) to TT. Similarly, in vitro priming of T cells with Id-pulsed DC resulted in marked increase in TNFalpha production (188 pg/ml), compared with unpulsed DC (<15 pg/ml). These data suggest that multiple in vitro immunization using DC as APC could be beneficial in generating tumor specific T cells from normal donor PBMC, which may be used for adoptive immunotherapy (e.g. donor lymphocyte infusion) of B cell malignancies. Thus, in vitro immunization can be a better alternative approach than immunization of stem cell transplant donor with tumor antigen.

L4 ANSWER 11 OF 79 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:300013 BIOSIS
DOCUMENT NUMBER: PREV200100300013
TITLE: Differential cytokine profiles of leukaemic blasts and leukaemic dendritic cells: Implications for immunotherapy.
AUTHOR(S): Panoskaltsis, Nicki (1); Knight, Stella C. (1); Reid, Cecil D. L.
CORPORATE SOURCE: (1) Antigen Presentation Research Group, Imperial College at Northwick Park Institute for Medical Research, Harrow UK
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 2, pp. 215b. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Dendritic cells (DCs) generated from leukaemic blasts are being evaluated for use in the immunotherapy of leukaemia. DCs can be cultured from most subtypes of AML blasts in approximately 50-75% of samples. These leukaemic DCs (LDCs) are derived from the leukaemic clone and are similar to mature DCs in their expression of surface markers and in their capacity to stimulate lymphocytes. However, stimulation of cytotoxicity against the original AML blasts using T cells expanded with LDCs has had limited success. These cytotoxicity results may be partly explained by the different methods used to generate the LDCs, in particular, the cytokines used in the culture. AML bone marrow mononuclear cells were cultured in serum-free medium for 4-5 and 13-14 days in the presence of granulocyte-macrophage colony stimulating factor and stem cell factor and supplemented with one of the following cytokines: tumour necrosis factor(TNF)-alpha, interleukin(IL)-4, IL-12, or flt-3 ligand (FL). Cells were evaluated by flow cytometry for DC surface markers, CD80, CD86, CD1a, CD40, CD11c, and HLA-DR, as well as for intracellular cytokines IL-4, IL-10, IL-12, and interferon(IFN)-gamma in the presence and absence of calcium ionophore, and the vesicular-transport inhibitor, monensin. Prior to culture, the AML blasts were skewed towards a type 2 cytokine profile, and in particular, showed IL-10 production out of proportion to the other cytokines. After culture, the cytokine profile of the LDC was influenced differentially, depending on the cytokine cocktails used. Exposure to TNF-alpha during the entire culture period, did not polarise the cells towards type 1 or type 2 cytokine production, but IL-4 caused the cultured cells to produce more IL-4. IL-12 exposure induced type 1 cytokines, namely IL-12 and IFN-gamma. In contrast, FL upregulated both type 1 and type 2 cytokines. Interestingly, IL-10 production by the leukaemic blasts was abrogated in all culture conditions. In one sample,

although IL-4 induced more IL-4 in the cells at day 5, the day 14
IFN-gamma expression increased to a fluorescence intensity beyond that of
the other samples. These results show that LDCs can be differentially
skewed towards a type 1 or type 2 profile, and imply that the cytokine
conditioning of these cells is critical for an effective anti-leukaemic
response.

L4 ANSWER 12 OF 79 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:299456 BIOSIS
DOCUMENT NUMBER: PREV200100299456
TITLE: In vitro priming of normal donor PBMC with myeloma protein
pulsed dendritic cells.
AUTHOR(S): Kim, S. B. (1); Baskar, S.; Kwak, L. W.
CORPORATE SOURCE: (1) Department of Medicine, Asan Medical Center, University
of Ulsan, Seoul South Korea
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp.
166a. print.
Meeting Info.: 42nd Annual Meeting of the American Society
of Hematology San Francisco, California, USA December
01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Dendritic cells (DC) are very efficient antigen-presenting cells (APC) and
have been used to directly present exogenous antigen to CD8+ T cells. In
vitro priming of T cells with DC pulsed with weak antigens such as tumor
idiotype (Id), is an attractive strategy to generate tumor-specific
cytotoxic T lymphocytes (CTL). A previous report from this laboratory
demonstrated generation of tumor-specific CTL using autologous DC pulsed
with patient Id (Blood, Oct. 15, 2000). In the present study, we extend
our investigation to generate antigen-specific T cells from normal donor
peripheral blood mononuclear cells (PBMC) by in vitro priming using
autologous DC as APC. After 2hr of incubation of PBMC, adherent cells were
cultured for generation of DC with IL-4 and GM-CSF, and DC were harvested
on different days. Phenotypic analysis showed that DC obtained at day 8,
day 10, and day 12 expressed high levels of HLA-DR.
The expression of CD80, CD83 and CD86, however, were higher in DC obtained
at day 8 compared to those at day 10 and day 12. We compared the ability
of DC to stimulate T cell cytokine responses to keyhole limpet
hemocyanin (KLH), tetanus toxoid (TT), and Id. In vitro primed T cells
(2-4 cycles of stimulation with Ag and DC) showed significant cytokine
responses (IFNgamma, TNFalpha, GM-CSF, IL-13) to TT. Similarly, in vitro
priming of T cells with Id-pulsed DC resulted in marked increase in
TNFalpha production (188 pg/ml), compared with unpulsed DC (< 15 pg/ml).
These data suggest that multiple in vitro immunization using DC as APC
could be beneficial in generating tumor specific T cells from normal donor
PBMC, which may be used for adoptive immunotherapy (e.g. donor lymphocyte
infusion) of B cell malignancies. Thus, in vitro immunization can be a
better alternative approach than immunization of stem cell transplantation
donor with tumor antigen.

L4 ANSWER 13 OF 79 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:503737 CAPLUS
DOCUMENT NUMBER: 133:88037
TITLE: Effects of IgG from patients with Graves'
ophthalmopathy and interferon-.gamma
. (IFN-.gamma.) on intercellular adhesion molecule-1,
HLA-DR expression of human retroocular fibroblasts
AUTHOR(S): Li, Yushu; Chen, Lei; Teng, Weiping; Shan, Zhongyan;
Li, Zhongmin
CORPORATE SOURCE: Department of Endocrinology, the First Clinical
College, China Medical University, Shenyang, 110001,
Peop. Rep. China
SOURCE: Zhonghua Neifenmi Daixie Zazhi (2000), 16(3), 146-149
CODEN: ZNDZEK; ISSN: 1000-6699
PUBLISHER: Shanghaishi Neifenmi Yanjiuso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The effects of IgG from the patients with Graves' ophthalmopathy (GO) and
IFN-.gamma. on the expressions of intercellular adhesion mol.-1 (ICAM-1),
HLA-DR on retroocular fibroblasts were assayed to study the possible
mechanism of humoral immunity and cellular immunity in the pathogenesis of
GO. The purified IgGs from 21 patients (10 cases of GO, 7 cases of
Graves' disease, 4 cases of toxic nodular goiter) and 8 normal subjects,
cytokine IFN-.gamma. and TSH (TSH) were incubated with normal human RFs in
vitro. Antigen expressions of RFs induced by stimulators were examd. by
flow cytometer after immunofluorescence staining. Normal RFs
spontaneously and partly expressed ICAM-1, but did not express HLA-DR.
All of the IgGs from the patients with GO and other thyroid disease and

normal subjects could not stimulate the expressions of ICAM-1
and HLA-DR of RFs. IFN-.gamma. and TSH significantly
enhanced the expression of ICAM-1 of RFs in dose-dependent manners (P <
0.05). Only IFN-.gamma. could stimulate RFs to express
HLA-DR (P < 0.05). IgG from the patients with GO could
not stimulate the expressions of ICAM-1 and HLA-
DR on the surface of cultured normal human RFs; IFN-.gamma. might
be the important factor for initiating and promoting autoimmune reactions
in GO; In addn., more attention should be paid to TSH which possibly plays
a promoting role in the pathogenesis of GO.

L4 ANSWER 14 OF 79 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:114570 BIOSIS
DOCUMENT NUMBER: PREV200000114570
TITLE: Characterization of tissue outgrowth developed in vitro in
patients with rheumatoid arthritis: Involvement of T cells
in the development of tissue outgrowth.
AUTHOR(S): Wakisaka, Sueshige; Suzuki, Noboru; Nagafuchi, Hiroko;
Takeba, Yuko; Kaneko, Atsushi; Asai, Tomiaki; Sakane,
Tsuyoshi (1)
CORPORATE SOURCE: (1) Departments of Immunology and Medicine, St. Marianna
University School of Medicine, 2-16-1, Sugao, Miyamae-ku,
Kawasaki, Kanagawa, 216-8511 Japan
SOURCE: International Archives of Allergy and Immunology, (Jan.,
2000) Vol. 121, No. 1, pp. 68-79.
ISSN: 1018-2438.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background: The aim of this study was to analyze cellular and cytokine
interactions governing the development of synovial tissue outgrowth in
patients with rheumatoid arthritis (RA). Methods: A single-cell suspension
of dissociated synovial tissues of RA patients was cultured for a long
period to develop tissue outgrowth. The resulting tissue outgrowth was
characterized by immunohistochemical staining and ELISA. Results: The
tissue outgrowth developed in vitro included various cell types, such as
macrophage-like synovial cells, fibroblast-like synovial cells and
lymphocytes. Even after prolonged cultivation, synovial cells devoid of
infiltrating T lymphocytes did not form tissue outgrowth. The outgrowth
contained CD3+ cells, LeuM3 (CD14)+ cells and HLA-DR+
cells. The T cells expressed lymphocyte function-associated antigen
(LFA)-1 and CD2, and the synovial cells expressed intracellular adhesion
molecule (ICAM)-1 and LFA-3, suggesting possible interactions via
LFA-1/ICAM-1 and CD2/LFA-3. Production of T-cell derived IFN-gamma and
IL-17 and synovial-cell-derived fibroblast growth factor (FGF)-1 and IL-15
was confirmed in the tissue outgrowth as well as in RA synovial tissue.
These cell types stimulate each other by secreting cytokines,
leading to the secretion of proinflammatory cytokines and matrix
metalloproteinase (MMP)-1 by the tissue outgrowth and proliferation of
both lymphocytes and synovial cells. Conclusion: This study emphasizes the
importance of cellular interactions between T cells and synovial cells,
via adhesion molecules and the secretion of cytokines with stimulatory
activity towards other cell types, for the hyperactivity of RA synovial
cells.

L4 ANSWER 15 OF 79 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:291475 BIOSIS
DOCUMENT NUMBER: PREV200100291475
TITLE: Anti-tumor CTL induction by exosomes secreted by human
dendritic cells.
AUTHOR(S): Takahashi, Masuhiro (1); Narita, Miwako; Liu, Aichun;
Kanda, Tatsuo; Fuse, Ichiro; Furukawa, Tatsuo; Toba, Ken;
Aizawa, Yoshifuwa
CORPORATE SOURCE: (1) School of Health Sciences, Faculty of Medicine, Niigata
University, Niigata Japan
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 33a.
print.
Meeting Info.: 42nd Annual Meeting of the American Society
of Hematology San Francisco, California, USA December
01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In order to establish an efficient cell-free immunotherapy for tumors, we
examined antigen presenting and CTL inducing functions of exosomes
secreted by human dendritic cells. Dendritic cells were generated by
culture of human peripheral adherent cells in serum-free, 1% autoserum or
10% FBS medium containing GM-CSF (100 ng/ml) and IL-4 (10 ng/ml) with or
without IFN-gamma (500 U/ml) or IL-10 (10 ng/ml). Dendritic cells were
generated also by the culture of peripheral blood mononuclear cells with
calcium ionophore, A23187 (375-750 ng/ml). Exosomes were prepared from

supernatants of dendritic cell culture by centrifugation method.
Supernatants were centrifuged at 10,000 g for eliminating cell debris and
then at 100,000 g for spinning down exosomes as pellets. For preparing
exosomes containing antigenic tumor peptides, dendritic cells, which were
generated from persons with HLA-A24 by culture in 1% autoserum containing
medium with GM-CSF and IL-4, were pulsed with 9mer SART-1 peptides
(donated by Dr. K Itoh, Kurume, Japan) on day 6 of culture and exosomes
were prepared on day 7. Antigen presenting function of exosomes were
evaluated by 3H-thymidine uptake of allogeneic lymphocytes cultured with
exosomes for 5 day. CTL inducing function of exosomes were evaluated by
51Cr-release assay using repeatedly exosome-primed, then IL-2 stimulated
autologous lymphocytes as effectors and KE4 (HLA-A24 positive and SART-1
expressing cell line) or the same dendritic cells pulsed with SART-1
peptides as targets. Dendritic cells cultured with GM-CSF & IL-4 with or
without IFN-gamma or IL-10 were demonstrated to secrete exosomes which
stimulate allogeneic lymphocyte proliferation. By culture of
peripheral blood mononuclear cells with A23187 for 4 days, dendritic cells
expressing CD83, CD80, CD86 and HLA-DR were generated
and were demonstrated to secrete exosomes which stimulate
allogeneic lymphocyte proliferation. Dendritic cells pulsed with SART-1
peptides were shown to secrete exosomes which induce CTL against KE4 or
autologous dendritic cells pulsed with the peptides. These findings
revealed that dendritic cell derived exosomes with antigen presenting and
CTL inducing function are applicable to anti-tumor immunotherapy.

L4 ANSWER 16 OF 79 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:317063 BIOSIS
DOCUMENT NUMBER: PREV200000317063
TITLE: Major peptide autoepitopes for nucleosome-specific T cells
of human lupus.
AUTHOR(S): Lu, Liangjun; Kaliyaperumal, Arunan; Boumpas, Dimitrios T.;
Datta, Syamal K. (1)
CORPORATE SOURCE: (1) Arthritis Division, Northwestern University Medical
School, 303 East Chicago Avenue, Ward 3-315, Chicago, IL,
60611-3008 USA
SOURCE: Journal of Clinical Investigation, (August, 1999) Vol. 104,
No. 3, pp. 345-355. print.
ISSN: 0021-9738.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We tested 154 peptides spanning the entire length of core histones of
nucleosomes for the ability to stimulate an anti-DNA
autoantibody-inducing T helper (Th) clone, as well as CD4+ T-cell lines
and T cells, in fresh PBMCs from 23 patients with lupus erythematosus. In
contrast to normal T cells, lupus T cells responded strongly to certain
histone peptides, irrespective of the patient's disease status.
Nucleosomal peptides in histone regions H2B10-33, H416-39 (and overlapping
H414-28), H471-94, and H391-105 (and overlapping H3100-114) were
recurrently recognized by CD4 T cells from the patients with lupus.
Remarkably, these same peptides overlap with major epitopes for the Th
cells that induce anti-DNA autoantibodies and nephritis in lupus-prone
mice. We localized 2 other recurrent epitopes for human lupus T cells in
H2A34-48 and H449-63. All the T-cell autoepitopes have multiple
HLA-DR binding motifs, and the epitopes are located in
histone regions recognized by lupus autoantibodies, suggesting a basis for
their immunodominance. Native nucleosomes and their peptides H416-39,
H471-94, and H391-105 induced a stronger IFN-gamma response, whereas
others, particularly, H2A34-48, favored an IL-10- and/or IL-4-positive
T-cell response. The major autoepitopes may reveal the mechanism of
autoimmune T-cell expansion and lead to antigen-specific therapy of human
lupus.

L4 ANSWER 17 OF 79 MEDLINE
DUPLICATE 7
ACCESSION NUMBER: 1999373628 MEDLINE
DOCUMENT NUMBER: 99373628 PubMed ID: 10444257
TITLE: T cell proliferation, MHC class II restriction and cytokine
products of gliadin-stimulated peripheral blood mononuclear
cells (PBMC).
AUTHOR: O'Keeffe J; Mills K; Jackson J; Feighery C
CORPORATE SOURCE: Department of Immunology, St James's Hospital, Dublin,
Ireland.. okeeffej@tcd.ie
SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1999 Aug) 117 (2)
269-76.
Journal code: 0057202. ISSN: 0009-9104.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990827
Last Updated on STN: 19990827
Entered Medline: 19990819

AB The immune response of PBMC to gliadin was investigated in patients with coeliac disease (CoD) by examining proliferation, MHC restriction and cytokine production. Gliadin induced low levels of proliferation in 63% of eight untreated patients, 32% of 28 treated patients and 35% of 31 healthy control subjects. In MHC restriction studies, the proliferative response to gliadin was inhibited (range 47-98% inhibition) in the presence of a MoAb to HLA-DR in each of three coeliac and three control donors studied. Using flow cytometry, increased expression of activation markers (HLA-DR and IL-2R) was demonstrated on gliadin-stimulated T cells from four of nine coeliac patients and three of seven healthy control donors. Cytokines were studied in culture supernatants using ELISA. Gliadin was a potent inducer of IL-6 and IL-10 in 100% of coeliac patients and controls, whereas IL-4 was not produced in either subject group. Gliadin induced IL-2 production in 40% of untreated patients, 42% of treated patients and 35% of healthy control donors. Interferon-gamma (IFN-gamma) in gliadin-stimulated cultures was found only in coeliac patients, observed in 33% of untreated patients and 25% of treated patients. Spontaneous secretion of both IL-2 and IFN-gamma was found more frequently in patients with untreated disease (87% of cases versus 21% of controls for IFN-gamma and 40% versus 0% for IL-2). These results suggest, as manifest by IFN-gamma production, that gliadin stimulates a Th1/Th0-like response in coeliac patients and a Th0-like response in healthy controls.

L4 ANSWER 18 OF 79 MEDLINE
DUPLICATE 8
ACCESSION NUMBER: 1998435876 MEDLINE
DOCUMENT NUMBER: 98435876 PubMed ID: 9764847
TITLE: Interleukin-17 and interferon-gamma synergize in the enhancement of proinflammatory cytokine production by human keratinocytes.
AUTHOR: Teunissen M B; Koomen C W; de Waal Malefyt R; Wierenga E A; Bos J D
CORPORATE SOURCE: Department of Dermatology, Academic Medical Center, University of Amsterdam, The Netherlands.
SOURCE: JOURNAL OF INVESTIGATIVE DERMATOLOGY, (1998 Oct) 111 (4) 645-9. Journal code: 0426720. ISSN: 0022-202X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981029
AB Keratinocytes are influenced by cytokines released by skin-infiltrating T lymphocytes. IL-17 is produced by activated CD4+ T cells and can stimulate epithelial cells. We investigated whether IL-17 could modulate the cytokine production and cell-surface molecule expression of keratinocytes. The effects of IL-17 were compared with those of IFN-gamma, which is also derived from activated T cells and is a strong stimulator for keratinocytes. IL-17 enhanced the mRNA and protein production of the proinflammatory cytokines IL-6 and IL-8 in a concentration-dependent way, and induced a weak expression of intercellular adhesion molecule (ICAM)-1 and HLA-DR. The production of IL-1alpha and IL-15 was not altered. IFN-gamma augmented the production of IL-6, IL-8, and IL-15 and strongly induced both cell-surface molecules. IL-17 and IFN-gamma showed marked synergism in the stimulation of IL-6 and IL-8 protein secretion and, to a lesser extent, in the induction of ICAM-1 and HLA-DR expression. The majority of the CD4+ and CD8+ T cell clones derived from lesional psoriatic skin expressed IL-17 mRNA, suggesting that skin-infiltrating T cells can produce this cytokine. This IL-17 mRNA expression was detectable in T helper cell type 1 and type 2 and did not correlate with the IFN-gamma or IL-4 production. In addition, IL-17 mRNA is detectable in biopsies from lesional psoriatic skin, but not in nonlesional control biopsies. Our study indicates that IL-17 is a proinflammatory cytokine, which could amplify the development of cutaneous inflammation and may support the maintenance of chronic dermatoses, through stimulation of keratinocytes to augment their secretion of proinflammatory cytokines.

L4 ANSWER 19 OF 79 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:523387 CAPLUS
DOCUMENT NUMBER: 129:244075
TITLE: Nurse-like cells from bone marrow and synovium of patients with rheumatoid arthritis promote survival and enhance function of human B cells
AUTHOR(S): Shimaoka, Yasunori; Attrep, Jeanne F.; Hirano, Toshio; Ishihara, Katsuhiko; Suzuki, Ryuji; Toyosaki, Tomoko; Ochi, Takahiro; Lipsky, Peter E.
CORPORATE SOURCE: Department of Orthopedic Surgery, Osaka University Medical School, Osaka, 565, Japan

SOURCE: Journal of Clinical Investigation (1998), 102(3), 606-618
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thymic nurse cells are known to interact with T cells and play a role in their functional maturation. However, the role of nurse cells in B cell maturation and differentiation is less well established, esp. at extra-lymphoid sites. To address this issue, nurse-like cell clones from bone marrow and synovial tissue of patients with RA (RA-NLC) were established and characterized. RA-NLC constitutively expressed CD29, CD49c, CD54 (ICAM-1), CD106 (VCAM-1), CD157 (BST-1), and class I MHC mols., and secreted IL-6, IL-7, IL-8, granulocyte-macrophage colony-stimulating factor (GM-CSF) and granulocyte colony-stimulating factor (G-CSF). Bone marrow-derived and synovial RA-NLC differed in that the former secreted IL-7 and expressed a greater d. of CD157 constitutively and after stimulation with IFN.gamma., whereas the latter secreted G-CSF and more IL-6. Stimulation of both bone marrow and synovial RA-NLC induced expression of CD40 and class II MHC, but not CD154 (CD40L) or CD35. RA-NLC rescued peripheral B cells from spontaneous apoptosis and promoted survival of B cells for > 4 wk. B cell survival was blocked by antibodies to CD106 or CD157. RA-NLC also increased Ig prodn. from B cells. After long-term culture (4-6 wk) with RA-NLC, but not alone or with fibroblasts, outgrowth of B cells was obsd. All B cell lines derived from these cultures had been transformed by EBV, although the RA-NLC themselves were not infected with EBV. Precursor frequency anal. indicated that .apprx. 1 in 12,500 peripheral B cells could give rise to these EBV-transformed B cell lines upon coculture with RA-NLC.
These results indicate that RA-NLC from bone marrow and synovium have the capacity to rescue B cells from spontaneous apoptosis, facilitate Ig prodn., and promote the outgrowth of EBV-transformed B lymphoblastoid cells. These findings suggest that RA-NLC may play a role in the local and systemic hyperreactivity of B cells characteristic of rheumatoid arthritis.
REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 79 MEDLINE
DUPLICATE 9
ACCESSION NUMBER: 1998279289 MEDLINE
DOCUMENT NUMBER: 98279289 PubMed ID: 9616317
TITLE: Protein transport and processing by human HT29-19A intestinal cells: effect of interferon gamma.
COMMENT: Comment in: Gut. 1998 Apr;42(4):455-6
AUTHOR: Terpend K; Boisgerault F; Blaton M A; Desjeux J F; Heyman M
CORPORATE SOURCE: INSERM U290, Hopital St Lazare, Paris, France.
SOURCE: GUT, (1998 Apr) 42 (4) 538-45.
Journal code: 2985108R. ISSN: 0017-5749.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980625
Last Updated on STN: 20021217
Entered Medline: 19980616
AB BACKGROUND: The nature of the breakdown products produced in enterocytes during epithelial transport of intact proteins may be critical in determining the functional consequences of protein absorption. AIM: (a) To measure the transepithelial transport of horseradish peroxidase (HRP) and to identify the nature of HRP breakdown products released on the basal side of enterocytes and (b) to assess the role of interferon gamma (IFN gamma) on HRP transport and processing. METHODS:
HT29-19A intestinal cells were used to assess transepithelial transport of HRP in Ussing chambers, and the nature of breakdown products in the basal compartment was analysed by high performance liquid chromatography (HPLC).
RESULTS: (1) In control conditions, [3H]HRP equivalent fluxes (3135 (219) ng/h per cm2; mean (SEM) comprised 50% amino acids, 40% peptides, and 10% intact HRP. Steric exclusion HPLC of the breakdown products indicated a wide range of molecular masses including a major peptide of about 1150 Da.
Lysosomal aspartyl and thiol proteases were expressed but no HLA -DR surface expression was noted, (2) At 48 to 72 hours after IFN gamma stimulation, [3H]HRP equivalent fluxes increased significantly (7392 (1433) ng/h per cm2) without modification of the relative proportions of amino acids, peptides, and intact HRP, and without modification of the distribution of breakdown products in HPLC. Lysosomal protease activities were not modified by IFN gamma but HLA-

DR expression was increased. CONCLUSION: Intestinal cells are able to process HRP into peptides potentially capable of stimulating the immune system. IFN gamma stimulates the transport and processing of HRP thus increasing the antigenic load in the intestinal mucosa.

L4 ANSWER 21 OF 79 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 1998432545 MEDLINE
DOCUMENT NUMBER: 98432545 PubMed ID: 9761378
TITLE: Inhibitory effect of pentoxifylline on HLA-DR expression and glycosaminoglycan synthesis by retrobulbar fibroblasts.
AUTHOR: Balazs C; Kiss H; Farid N R
CORPORATE SOURCE: III. Department of Medicine-Endocrinology, Kenezy Teaching Hospital, Debrecen, Hungary.
SOURCE: HORMONE AND METABOLIC RESEARCH, (1998 Aug) 30 (8) 496-9. Journal code: 0177722. ISSN: 0018-5043.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115 Last Updated on STN: 19990115 Entered Medline: 19981204
AB OBJECTIVE: Glycosaminoglycan (GAG) production by retro-ocular fibroblasts (REF) is increased in patients with thyroid-associated ophthalmopathy (TAO). Various cytokines stimulate REFs to proliferate and elaborate GAG, free oxygen radicals as well as induce HLA-DR expression on these cells. Pentoxifyllin (Ptx) regulates the production of several cytokines including tumor necrosis factor alpha (TNF-alpha), interleukin-1 (IL-1) and, interferon gamma (IFN-gamma). We wished in this study to determine whether Ptx modified the spontaneous and cytokine-induced GAG synthesis by REF and IFN-gamma induced HLA-DR expression. DESIGN: REF derived from extraocular muscles of healthy subjects were cultured without and with cytokines (IFN-gamma, TNF alpha and IL-1) and the effect of Ptx on the production of GAG by REF and HLA-DR expression was determined. MEASUREMENTS: Glycosaminoglycan was measured by incorporation of (3H) glycosamine into GAG. HLA-DR expression was analyzed by fluorescence activated cell sorter. RESULTS: Both spontaneous and cytokine induced GAG synthesis by REF was inhibited by Ptx (100, 500 and 1000 mg/l, respectively). IFN-gamma (50, 100 and 500 U/ml) induced a dose-dependent increase in the expression of HLA-DR molecules by REF. Ptx, which was not toxic to REF, inhibited HLA-DR expression on those cells dose-dependently. CONCLUSIONS: Our in vitro results suggest that Ptx reduces cytokine-induced GAG production and HLA-DR expression by REF. It thus has potential as a therapeutic agent which regulates the function of lymphocytes infiltrating the retro-orbital tissues, and which are instrumental in TAO.

L4 ANSWER 22 OF 79 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:351412 CAPLUS
DOCUMENT NUMBER: 127:80067
TITLE: Distinct mechanisms of immunosuppression as a consequence of major surgery
AUTHOR(S): Hensler, Thorsten; Hecker, Heike; Heeg, Klaus; Heidecke, Claus-Dieter; Bartels, Holger; Barthlen, Winfried; Wagner, Hermann; Siewert, Jorg-Rudiger; Holzmann, Bernhard
CORPORATE SOURCE: Department Surgery, Klinikum rechts der Isar, Technical University, Munich, D-81675, Germany
SOURCE: Infection and Immunity (1997), 65(6), 2283-2291 CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Altered host defense mechanisms after major surgery or trauma are considered important for the development of infectious complications and sepsis. In the present study, we demonstrate that major surgery results in a severe defect of T-lymphocyte proliferation and cytokine secretion in response to coligation of the antigen receptor complex and CD28. During the early postoperative course, reduced cytokine secretion was obsd. for interleukin-2 (IL-2), gamma interferon, and tumor necrosis factor alpha, which are assocd. with the Th1 phenotype of helper T lymphocytes, and for IL-4, the index cytokine of Th2 cells. During the late postoperative course, T-cell cytokine secretion increased to normal levels. Prodn. of the anti-inflammatory cytokine IL-10 was altered, with different kinetics being selectively elevated during the late postoperative course. In contrast, the capacity of peripheral blood monocytes to present bacterial superantigens and to stimulate T-cell proliferation was normal

or enhanced after surgery despite a significant loss of cell surface
HLA-DR mols. Thus, the level of major
histocompatibility complex class II protein expression does not appear to
predict the antigen-presenting capacity of monocytes obtained from
surgical patients with uneventful postoperative recovery. Secretion of
IL-1.beta. and IL-10 by endotoxin-stimulated peripheral blood monocytes
was increased at different time points after surgery. Major surgery
therefore results in a distinct pattern of immune defects with a
predominant defect in the T-cell response to T-cell receptor- and CD28
coreceptor-mediated signals rather than an impaired monocyte
antigen-presenting capacity. Suppression of T-cell effector functions
during the early phase of the postoperative course may define a state of
impaired defense against pathogens and increased susceptibility to
infection and septic complications.

L4 ANSWER 23 OF 79 MEDLINE
DUPLICATE 11
ACCESSION NUMBER: 97436557 MEDLINE
DOCUMENT NUMBER: 97436557 PubMed ID: 9292530
TITLE: Myeloma bone marrow plasma cells: evidence for their
capacity as antigen-presenting cells.
AUTHOR: Yi Q; Dabadghao S; Osterborg A; Bergenbrant S; Holm G
CORPORATE SOURCE: Department of Medicine, Karolinska Hospital, Stockholm,
Sweden.
SOURCE: BLOOD, (1997 Sep 1) 90 (5) 1960-7.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19971013
Last Updated on STN: 20021218
Entered Medline: 19970930
AB Myeloma plasma cells constitute 10% to 90% of the total bone marrow cell
count in patients with multiple myeloma (MM). These cells express a
variety of cell surface markers, such as HLA-ABC and HLA-
DR, and surface antigens that are necessary for professional
antigen-presenting cells, including adhesion and costimulatory molecules.
In this study, we examined the expression of major histocompatability
complex (MHC) and costimulatory molecules on CD38(bright,++) plasma cells
in bone marrow aspirates from eight MM patients. Small percentages of
plasma cells expressed weak but detectable levels of HLA-
DR, HLA-DQ, CD40, CD80, and CD86, which could be upregulated by
interferon-gamma (IFN-gamma) and tumor necrosis
factor-alpha. CD38++ plasma cell and CD38(dim,+) cells were sorted from
freshly isolated bone marrow mononuclear cells and tested for their
capacity to act as antigen-presenting cells. Indeed, both CD38++ plasma
cells and CD38+ cells were able to stimulate allogeneic T cells
and present the soluble antigens purified protein derivative and tetanus
toxoid to autologous T cells. Recognition of the antigens led to T-cell
proliferation and secretion of IFN-gamma and was MHC class-I and -II
restricted. Antigen processing and presentation by CD38++ and CD38+ cells
were abolished by treatment of the cells with chloroquine. Hence, our
study provides for the first time evidence that myeloma plasma cells may
act as antigen-presenting cells. Further studies are warranted to examine
in detail the molecules required for inducing T-cell stimulation.

L4 ANSWER 24 OF 79 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:365639 CAPLUS
DOCUMENT NUMBER: 127:60351
TITLE: Beta-sitosterol and beta-sitosterol glucoside
stimulate human peripheral blood lymphocyte
proliferation: implications for their use as an
immunomodulatory vitamin combination
AUTHOR(S): Bouic, P. J. D.; Etsebeth, S.; Liebenberg, R. W.;
Albrecht, C. F.; Pegel, K.; Van Jaarsveld, P. P.
CORPORATE SOURCE: Departments of Medical Microbiology and Pharmacology,
Faculty of Medicine, University of Stellenbosch,
Tygerberg, 7505, S. Afr.
SOURCE: International Journal of Immunopharmacology (1997),
Volume Date 1996, 18(12), 693-700
CODEN: IJIMDS; ISSN: 0192-0561
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The phytosterols, .beta.-sitosterol (BSS), and its glucoside (BSSG)
enhance the in vitro proliferative response of T-cells stimulated by
sub-optimal concns. of phytohemagglutinin (PHA) several fold at extremely
low concns. (femtogram level). A 100:1 (mass:mass) ratio of BSS:BSSG
(termed essential sterolin formulation, ESF) showed higher stimulation
than the individual sterols at the same concn. In vivo activity of ESF
was also demonstrated when volunteers ingested ESF for 4 wk.

Proliferation of their T-cells, stimulated maximally with PHA, was
significantly enhanced (20-920%) when compared to baseline values. In
vitro, ESF (1 .mu.g/mL) was able to significantly enhance the expression
of CD25 and HLA-Dr activation antigens on T-cells and increased the
secretion, into the medium, of IL-2 and gamma interferon. NK-cell
activity was also increased by BSS and BSSG alone, but with ESF a higher
activity was always found at different effector:target ratios
(100:1-12:1).

L4 ANSWER 25 OF 79 MEDLINE
DUPLICATE 12
ACCESSION NUMBER: 97319193 MEDLINE
DOCUMENT NUMBER: 97319193 PubMed ID: 9176096
TITLE: T-cell cytokines may control the balance of functionally
distinct macrophage populations.
AUTHOR: Tormey V J; Faul J; Leonard C; Burke C M; Dilmec A; Poulter
L W
CORPORATE SOURCE: Department of Clinical Immunology, Royal Free Hospital
School of Medicine, London, UK.
SOURCE: IMMUNOLOGY, (1997 Apr) 90 (4) 463-9.
Journal code: 0374672. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970709
Last Updated on STN: 19970709
Entered Medline: 19970623
AB As monocytes differentiate into mature macrophages, subsets emerge that
exhibit stimulatory, suppressive or phagocytic potential. These
functionally distinct subsets can be discriminated using monoclonal
antibodies RFD1 and RFD7. As examples of all these subsets have been
repeatedly identified within the macrophage pool in a variety of organs
the overall functional capacity of this pool will depend on the relative
balance of these subpopulations. This study investigates whether this
balance present in mature macrophage populations can be regulated by the
local influence of T-cell-derived cytokines. The dose-dependent effect of
cytokines interferon-gamma (IFN-gamma), interleukins
(IL) IL-2, IL-4 and IL-10 on the phenotype and function of
monocyte-derived macrophages was determined. Subsets of mature cells were
quantified by identifying RFD1- RFD7- stimulatory cells (D1+); RFD1- RFD7+
phagocytes (D7+) and RFD1+ RFD7+ suppressive cells (D1 D7+). IFN-gamma and
IL-4 increased the relative proportions of D1+ stimulatory cells and
upregulated HLA-DR expression. IFN-gamma also
increased the capacity of the mature macrophage pool to stimulate
T-cell proliferation. IL-10 reduced the proportions of D1+ stimulatory
cells while promoting the differentiation of D7+ phagocytes and D1/D7+
suppressive cells. IL-10 induced changes also reduced the functional
capacity of the mature populations to stimulate T cells in auto
and allogenic mixed lymphocyte reactions (MLR). IL-2 had no effect on
differentiation of monocytes. Thus IL-4 and IFN-gamma are seen to induce
the development of stimulatory macrophages while IL-10 promotes
differentiation of monocytes to mature phagocytes and suppressive
macrophages. It is concluded that mature macrophage phenotype is 'plastic'
and under the control of T-cell-derived mediators. Furthermore, within the
differentiating monocytes, phenotypic change appears to carry with it
functional change, thus retaining the relationship between antigen
expression and activity in the mature macrophage populations.

L4 ANSWER 26 OF 79 MEDLINE
DUPLICATE 13
ACCESSION NUMBER: 97471725 MEDLINE
DOCUMENT NUMBER: 97471725 PubMed ID: 9330666
TITLE: Inhibitory effect of pentoxifylline on HLA-DR expression
and glycosaminoglycan synthesis of retrobulbar fibroblasts
induced by interferon gamma.
AUTHOR: Balazs C; Kiss E; Farid N R
CORPORATE SOURCE: III. Department of Medicine-Endocrinology, Kenezy Teaching
Hospital, Debrecen, Hungary.
SOURCE: ACTA MICROBIOLOGICA ET IMMUNOLOGICA HUNGARICA, (1997) 44
(2) 173-9.
Journal code: 9434021. ISSN: 1217-8950.
PUB. COUNTRY: Hungary
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971113
AB Glycosaminoglycan (GAG) accumulation produced by retroocular fibroblasts
(REF) has been observed in patients with thyroid-associated ophthalmopathy
(TAO). Various cytokines are able to express HLA-DR
molecules and stimulate the REF to proliferate GAG and free
oxygen radicals. Pentoxifylline (Ptx) is known to have complex

immunomodulatory effects on production of cytokines including
interferon gamma (IFN-gamma). Ptx has been assumed to
inhibit the cytokine-induced production of GAG and HLA-
DR expression. We wished to determine whether Ptx has an effect on
the IFN-gamma induced HLA-DR expression and influences
the spontaneous and cytokine-induced GAG synthesis of REF. REF derived
from extraocular muscles of healthy subjects were cultured without and
with IFN-gamma. The effect of Ptx on expression of HLA-
DR molecules and the production of GAG by REF was determined.
Glycosaminoglycan was measured by incorporation of (3H)glycosamine into
GAG. HLA-DR expression was analysed by fluorescence
activated cell sorter. IFN-gamma (50, 100 and 500 U/ml) induced an
increase in expression of HLA-DR molecules of REF. Ptx
was proved not to be toxic for cultured cells. This drug was able to
dose-dependently inhibit HLA-DR expression of REF.
Both spontaneous and IFN-gamma-induced GAG synthesis of REF was inhibited
by Ptx (100, 500 and 1000 mg/l, respectively). Due to in vitro inhibitory
effects, Ptx is potentially able to modify the antigen presentation and
the GAG synthesis by REF and it might be a useful therapeutical drug in
the treatment of TAO.

L4 ANSWER 27 OF 79 MEDLINE
DUPLICATE 14
ACCESSION NUMBER: 97222552 MEDLINE
DOCUMENT NUMBER: 97222552 PubMed ID: 9069581
TITLE: Differential effects of human interferon alpha and
interferon gamma on xenografted human
thyroid tissue in severe combined immunodeficient mice and
nude mice.
AUTHOR: Kawai K; Enomoto T; Fornasier V; Resetkova E; Volpe R
CORPORATE SOURCE: Endocrinology Research Laboratory, Wellesley Hospital,
University of Toronto, Ontario, Canada.
SOURCE: PROCEEDINGS OF THE ASSOCIATION OF AMERICAN PHYSICIANS,
(1997 Mar) 109 (2) 126-35.
Journal code: 9514310. ISSN: 1081-650X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970612
Last Updated on STN: 20000303
Entered Medline: 19970603

AB We have studied the in vivo effects of human interferon alpha (IFN-alpha)
and interferon gamma (IFN-gamma) administration on
human thyroid tissue xenografted into two mouse strains: severe combined
immunodeficient (SCID) mice and nude mice. Human lymphocytes survive in
SCID mice but are lysed in nude mice. Thyroid tissues from Graves' disease
or Hashimoto's thyroiditis, or paranodular [normal, (N)] tissue was
xenografted into SCID mice (0.8 g/mouse) pretreated with anti-asialo GM-1
antiserum and radiation and also into nude mice. One week after
xenografting, SCID and nude mice were divided into three groups. Group A
was treated with IFN-alpha intraperitoneally (2,000 units/mouse) three
times weekly; group B was treated with IFN-gamma similarly; group C was
treated with phosphate buffered saline (PBS) only (control). Autologous
human peripheral blood mononuclear cells (PBMCs) were added to mice
receiving N xenografts. Blood was taken every 2 weeks for levels of IgG
and thyroid antibodies (TAb). After 6 weeks of treatment, mice were
sacrificed, and xenograft thyrocyte histocompatibility leukocyte antigen (
HLA-DR) and intercellular adhesion molecule (ICAM-1)
expression were measured. In addition, thyrocyte cultures were stimulated
in vitro with 200 units/ml of either IFN-alpha or IFN-gamma or PBS
(control). SCID mice xenografted with autoimmune thyroid disease (AITD) in
group A showed a significantly higher TAb production than group C, whereas
in group B, TAb production was not statistically increased compared to
control (group C). SCID mice xenografted with N did not produce TAb in any
group, nor did nude mice xenografted with AITD. Thyrocyte HLA-
DR expression was markedly increased in group A and B in SCID mice
xenografted with Graves' disease, Hashimoto's thyroiditis, and N tissue
compared to group C. In contrast, only group B (IFN-gamma) showed an
increase in thyrocyte HLA-DR in nude mice. In the in vitro studies, only IFN-gamma (not IFN-alpha) stimulated thyrocyte
HLA-DR and ICAM-1 expression in Graves' disease, Hashimoto's thyroiditis, and N tissues. We concluded that in SCID mice,
IFN-alpha causes TAB production in AITD xenografts but not in N
xenografts, while increasing thyrocyte HLA-DR expression in both. Also, IFN-gamma does not cause a statistically
increased TAb in AITD xenografts in SCID mice, despite a sharp rise in
thyrocyte HLA-DR expression. In addition, because IFN-alpha has no effect in nude mice or in vitro on thyrocyte HLA

-DR expression, its effects in SCID mice must be mediated via
local infiltrating lymphocytes. Finally, IFN-gamma has a direct effect on
thyrocytes to increase HLA-DR expression (and, in vitro, ICAM-1 expression) but may not stimulate TAb production.

L4 ANSWER 28 OF 79 MEDLINE
DUPLICATE 15
ACCESSION NUMBER: 97174265 MEDLINE
DOCUMENT NUMBER: 97174265 PubMed ID: 9021999
TITLE: Antigen presentation by interferon-gamma
-treated thyroid follicular cells inhibits interleukin-2
(IL-2) and supports IL-4 production by B7-dependent human T
cells.
AUTHOR: Lombardi G; Arnold K; Uren J; Marelli-Berg F; Hargreaves R;
Imami N; Weetman A; Lechler R
CORPORATE SOURCE: Department of Immunology, Royal Postgraduate Medical
School, London, GB..
glombard@rpms.ac.uk
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1997 Jan) 27 (1) 62-71.
Journal code: 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970313
Last Updated on STN: 19970313
Entered Medline: 19970305
AB The consequence of recognition of antigen on antigen-presenting cells that
are induced to express major histocompatibility complex (MHC) class II
molecules following an inflammatory process is still not clear. In this
study, we have investigated the outcome of antigen presentation by
epithelial cells and we have used as a model thyroid follicular cells
(TFC) that are known to express MHC class II molecules in autoimmune
thyroid diseases and acquire the capacity to present autoantigens to T
cells infiltrating the thyroid gland. The result show that MHC class
II-expressing TFC were unable to stimulate a primary T cell
alloresponse, using CD4+ T cells from three HLA-mismatched responders.
Phenotypic analysis showed that TFC, after incubation with
interferon-gamma, do not express the costimulatory molecules B7-1 (CD80) and -2 (CD86). Addition of murine DAP.3 cells
expressing human B7-1 (DAP.3-B7) to cultures containing peripheral blood
CD4+ T cells and DR1-expressing TFC led to a proliferative response,
suggesting that the failure of TFC to stimulate a primary
alloresponse was due to a lack of co-stimulation. Similarly, HLA
-DR-restricted, influenza-specific T cell clones dependent on B7
for co-stimulation did not respond to peptide presented by TFC; again the
lack of response could be overcome by co-culture of TFC with DAP.3-B7.
Furthermore, recognition of antigen on TFC inhibited interleukin-2 (IL-2)
production in the B7-dependent T cells. In contrast, in T helper type 0
(Th0) T cells, IL-4 release was not affected by TFC presentation. In
addition, antigen presentation by TFC favored IL-4 production relative to
IL-2 production by B7-independent Th0 clones. These results suggest that
antigen presentation by MHC class II+ TFC may induce tolerance in
autoreactive Th1 cells but may simultaneously favors a Th2 response in
uncommitted T cells, and thereby support autoantibody production.

L4 ANSWER 29 OF 79 MEDLINE
DUPLICATE 16
ACCESSION NUMBER: 97083790 MEDLINE
DOCUMENT NUMBER: 97083790 PubMed ID: 8930134
TITLE: Transforming growth factor-beta inhibits interferon
-gamma-induced HLA-DR expression by cultured
human fibroblasts.
AUTHOR: Armendariz-Borunda J; Endres R O; Ballou L R; Postlethwaite
A E
CORPORATE SOURCE: Institute of Molecular Biology in Medicine, CUCS,
University of Guadalajara, Jal, Mexico.
SOURCE: INTERNATIONAL JOURNAL OF BIOCHEMISTRY AND CELL BIOLOGY,
(1996 Oct) 28 (10) 1107-16.
Journal code: 9508482. ISSN: 1357-2725.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961231
AB This study shows the induction of HLA-DR (DR) in fibroblasts by IFN-gamma and investigates the molecular mechanisms
involved in the further DR down-regulation by TGF-beta 1. Kinetics of DR
induction on human dermal fibroblasts by IFN-gamma showed that 1 hr of
exposure was required to induce detectable levels of DR, and maximal DR
expression was achieved only after 2 days of exposure to IFN-gamma.
TGF-beta 1 inhibited DR induction by IFN-gamma, although complete

inhibition never could be achieved, even with high concentrations of
TGF-beta 1 and low concentrations of IFN-gamma. Inhibition was not
accounted for by reduction in cell numbers, as TGF-beta 1 stimulated
growth of the fibroblasts. Inhibition of DR induction was seen only if
TGF-beta 1 was added during the first 24 hr of IFN-gamma treatment.
TGF-beta 1 inhibited equally well if the cells were pretreated for as
little as 1 hr and then washed before addition of IFN-gamma. TGF-beta 1
did not cause an overall suppression of protein synthesis. Northern blot
analysis revealed that TGF-beta 1 greatly reduced the steady-state level
of DR beta mRNA induced by IFN-gamma at 24 hr, and then DRP transcripts
became undetectable at later stages. It is concluded that early
intracellular signals must build up to stimulate maximum DR
synthesis, which, later on, are inactivated or degraded by the action of
TGF-beta 1. We suggest that these mechanisms regulating DR gene
transcription involve the action of genes coding for specific
IFN-gamma-inducible transcriptional factors that are turned on and off in
an expeditious manner.

L4 ANSWER 30 OF 79 MEDLINE
DUPLICATE 17
ACCESSION NUMBER: 97081846 MEDLINE
DOCUMENT NUMBER: 97081846 PubMed ID: 8923089
TITLE: Current and future clinical applications of
interferon-gamma in host antimicrobial defense.
AUTHOR: Murray H W
CORPORATE SOURCE: Department of Medicine, Cornell University Medical College,
New York, NY 10021, USA.
CONTRACT NUMBER: AI 16963 (NIAID)
SOURCE: INTENSIVE CARE MEDICINE, (1996 Oct) 22 Suppl 4 S456-61.
Ref: 21
Journal code: 7704851. ISSN: 0342-4642.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970305
Last Updated on STN: 19970305
Entered Medline: 19970214
AB The T cell-derived macrophage-activating lymphokine, interferon-
gamma (IFN-gamma), is the most broadly acting antimicrobial-
inducing and host defense-enhancing cytokine thus far identified in
experimental models of infectious diseases. The activity induced by
IFN-gamma encompasses all classes of non-viral pathogens including
intracellular and extracellular parasites, fungi and bacteria. In man,
treatment with immuno-enhancing doses of IFN-gamma is safe, well-tolerated
and stimulates the antimicrobial mechanisms of blood monocytes,
circulating neutrophils and tissue macrophages. Aerosol administration
activates alveolar macrophages in a compartmentalized fashion. Monocytes
from IFN-gamma-treated patients with cancer, leprosy, and AIDS all respond
with the activated phenotype, and suppressed monocyte HLA-
DR expression in trauma patients can be up-regulated by IFN-gamma
therapy. Thus far, IFN-gamma has been recognized as effective in the
prophylaxis of chronic granulomatous disease and as adjunctive treatment
in at least one systemic intracellular infection, visceral leishmaniasis.
Additional trials suggest beneficial effects as prophylaxis in trauma and
as treatment in leprosy, cutaneous leishmaniasis, and HIV- and
non-HIV-related disseminated atypical mycobacterial infection. IFN-gamma
is also being tested as a prophylaxis in patients with burns and advanced
HIV infection and as an adjunct in drug-resistant tuberculosis. Future
antimicrobial applications for IFN-gamma include: a) long-term prophylaxis
in T cell-deficient states, b) short-term prophylaxis in patients with a
reversible host defense defect such as granulocytopenia or immune response
suppression induced by trauma or burn injury, and c) adjunctive treatment
along with conventional antibiotic therapy for i) nosocomial pneumonia
(aerosol administration), ii) opportunistic infections in general, iii)
infections which typically respond poorly to available treatment and iv)
for infections which require prolonged therapy for cure. In the latter,
the addition of IFN-gamma may accelerate the response to conventional
therapy and permit a clinically important reduction in the duration of
treatment while preserving efficacy.

L4 ANSWER 31 OF 79 MEDLINE
DUPLICATE 18
ACCESSION NUMBER: 96370466 MEDLINE
DOCUMENT NUMBER: 96370466 PubMed ID: 8774362
TITLE: Staphylococcal enterotoxin B-specific adhesion of murine
splenic T cells to a human endothelial cell line.
AUTHOR: Kita M; Eguchi K; Kawabe Y; Tsukada T; Migita K; Kawakami
A; Matsuoka N; Nagataki S

CORPORATE SOURCE: First Department of Internal Medicine, Nagasaki University
School of Medicine, Japan.
SOURCE: IMMUNOLOGY, (1996 Jul) 88 (3) 441-6.
Journal code: 0374672. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961015
Last Updated on STN: 19961015
Entered Medline: 19961002

AB The presence of a putative autoantigen of autoimmune disorder in a target organ may cause accumulation of specific T cells in the inflammatory region. One of the mechanisms of such accumulation involves the migration of specific-circulating T cells through the endothelial cells into the target lesion. The presence of only a few specific T cells responsive to a putative autoantigen has hampered the investigation of specific migration of circulating T cells to the target organ. We used a superantigen to investigate specific T-cell adhesion to endothelial cells, because it stimulates a large proportion of T cells with particular V beta elements and adhesion of T cells to the endothelium is a vital step in the migration process. Adhesion of murine T cells to the human endothelial cell line, EA.hy926, was specifically increased in the presence of staphylococcal enterotoxin B (SEB). The increase was interferon-gamma (IFN-gamma)-dependent, and consisted mainly of CD4+ T cells. V beta 8.1,2+ T cells preferentially adhered to endothelial cells in the presence of SEB compared with V beta 6+ T cells. Pretreatment of endothelial cells with SEB increased the adherence of V beta 8.1,2+ T cells, while anti-human leucocyte antigen (HLA)-DR and -DQ antibodies inhibited the increased adherence of V beta 8.1,2+ T cells. Our results demonstrate that increased T-cell adhesion to endothelial cells is SEB specific, and that the specificity is dependent on major histocompatibility complex (MHC) class II molecules expressed on endothelial cells and on the recognition of the SEB-MHC class II complex by V beta 8.1,2+ T cells.

L4 ANSWER 32 OF 79 MEDLINE
DUPLICATE 19
ACCESSION NUMBER: 96180265 MEDLINE
DOCUMENT NUMBER: 96180265 PubMed ID: 8599973
TITLE: Constitutive production of colony-stimulating factors by human hepatoma cell lines: possible correlation with cell differentiation.
AUTHOR: Wang S Y; Chen L Y; Tsai T F; Su T S; Choo K B; Ho C K
CORPORATE SOURCE: Department of Medical Research, Veterans General Hospital-Taipei, Taiwan, Republic of China.
SOURCE: EXPERIMENTAL HEMATOLOGY, (1996 Feb) 24 (3) 437-44.
Journal code: 0402313. ISSN: 0301-472X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199604
ENTRY DATE: Entered STN: 19960513
Last Updated on STN: 19970203
Entered Medline: 19960426

AB A panel of two poorly differentiated (HA22T/VGH and SK-Hep-1) and six well-differentiated (HuH-6-cl 5, HuH-7, PLC/PRF/5, Hep G2, Hep 3B, and Tong) human hepatocellular carcinoma (HCC) cell lines were studied for the production of colony-stimulating factors (CSFs) using the granulocyte and macrophage colony formation (CFU-GM) assay, immunocytochemical staining, and Northern blotting. Medium conditioned by untreated HA22T/VGH cells contained a high level of CSFs that could stimulate the in vitro colony formation of human myeloid progenitor cells. The HA22T/VGH cell-derived CSF had an apparent molecular weight of 23 kD. Its activity could be effectively neutralized by antiserum against granulocyte-macrophage CSF (GM-CSF) but not by antibodies to other hematopoietic growth factors, including G-CSF, M-CSF, interleukin-3 (IL-3), and IL-6. Correspondingly, immunocytochemical studies using monoclonal anti-GM-CSF showed a strong positive reaction in the cytoplasm of the HA22T/VGH cells. Northern blot analysis revealed that untreated HA22T/VGH cells expressed a considerable amount of GM-CSF mRNA, confirming that GM-CSF production was constitutive. At optimal concentrations, lipopolysaccharide (LPS), IL-1beta, interferon-gamma (IFN-gamma), and tumor-promoting phorbol diester (TPA) could all stimulate HA22T/VGH cells to secrete GM-CSF. In addition to HA22T/VGH, SK-Hep-1 cells could also produce GM-CSF, although less effectively, whereas all the well-differentiated HCC cell lines tested were negative for CSF production. Morphologic, cytochemical, and immunocytochemical examinations demonstrated that both poorly differentiated CSF-producing HCC cell lines (HA22T/VGH and SK-Hep-1) were macrophage-like in morphology, possessed

nonspecific esterase (NSE) activity, and expressed CD14, CD68, and HLA-DR on their surface, while all the well-differentiated HCC cell lines were epithelioid and lacked myeloid differentiation antigens. These results suggest that monocytoid features and CSF production may be differentiation markers of hepatocytes at the immature stages, amd that the HA22T/VGH and SK-Hep-1 cell lines may be valuable tools for the study of hepatic function and differentiation.

L4 ANSWER 33 OF 79 MEDLINE
DUPLICATE 20
ACCESSION NUMBER: 97180617 MEDLINE
DOCUMENT NUMBER: 97180617 PubMed ID: 9028793
TITLE: Human keratinocytes constitutively express IL-4 receptor molecules and respond to IL-4 with an increase in B7/BB1 expression.
AUTHOR: Junghans V; Jung T; Neumann C
CORPORATE SOURCE: Department of Dermatology, University of Gottingen, Germany.
SOURCE: EXPERIMENTAL DERMATOLOGY, (1996 Dec) 5 (6) 316-24.
Journal code: 9301549. ISSN: 0906-6705.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970630
Last Updated on STN: 19980206
Entered Medline: 19970619
AB In certain pathological conditions, such as atopic dermatitis, interleukin-4 (IL-4) can be detected in the skin. As the role of this cytokine in inflammatory skin lesions is not completely clear, we investigated its biological effects on skin keratinocytes. It was found that freshly isolated as well as cultured keratinocytes obtained from normal individuals express mRNA for the IL-4 receptor (IL-4R) and produce IL-4R protein, as determined by flow cytometry. Moreover, IL-4 induced a proliferative response in keratinocytes after 1 day of culture and enhanced B7/BB1 expression in these cells. B7-2 (CD86) mRNA and protein were neither detected on untreated nor IL-4 treated keratinocytes. In contrast to interferon-gamma (IFN-gamma), IL-4 did not induce ICAM-1 (CD54) or HLA-DR-expression. Keratinocytes which had been treated with IL-4 showed an enhanced ability to stimulate allogeneic T-cell proliferation in the presence of staphylococcus enterotoxin B (SEB), ($p < 0.01$). Neutralizing anti-B7/BB1 monoclonal antibodies did not block this effect. These results indicate that other molecules than B7/BB-1. HLA-DR or ICAM-1 on IL-4-activated keratinocytes may be involved in T-cell stimulation. In conclusion our results suggest that locally produced IL-4, besides modulating keratinocyte membrane molecules, may enable keratinocytes to interact with skin infiltrating lymphocytes.

L4 ANSWER 34 OF 79 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:626195 CAPLUS
DOCUMENT NUMBER: 125:273544
TITLE: Alloproliferation of purified CD4+ T cells to adult human heart endothelial cells, and study of second-signal requirements
AUTHOR(S): McDouall, R. M.; Page, C. S.; Hafizi, S.; Yacoub, M. H.; Rose, M. L.
CORPORATE SOURCE: National Heart Lung Inst. (Imperial College), Harefield Hosp., Middlesex, UK
SOURCE: Immunology (1996), 89(2), 220-226
CODEN: IMMUAM; ISSN: 0019-2805
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human endothelial cells have been shown to be capable of causing direct allostimulation of T cells. However, the majority of immunol. studies of human endothelial cells have been performed on cells of fetal origin. Here we use endothelial cells isolated from the adult human heart, both large vessel (coronary artery, pulmonary artery and aorta) and also microvascular. We have examd. the ability of all these endothelial cells to cause direct allostimulation of T cells, and show that purified CD4+ T cells can proliferate in response to adult human heart endothelial cells, the response being dependent on pretreatment of the endothelial cells with interferon-.gamma. (IFN-.gamma.) and inhibited by anti-HLA-DR monoclonal antibody. The proliferative responses of CD8+ T cells to adult but not fetal endothelial cells was inconsistent and weak. Proliferative responses were not blocked by CTLA4-Ig, which inhibits T-cell responses to 'classical' antigen-presenting cells (APC), but >50% inhibition was achieved with monoclonal antibody to lymphocyte function-assocd. antigen-3 (LFA-3). These results show that adult human cardiovascular endothelial cells are capable of causing allostimulation of resting CD4+ T cells, using a different second signal to classical APC. In view of these findings, endothelial cells should be considered as APC

following solid organ transplantation.

L4 ANSWER 35 OF 79 MEDLINE
DUPLICATE 21
ACCESSION NUMBER: 96409610 MEDLINE
DOCUMENT NUMBER: 96409610 PubMed ID: 8814591
TITLE: Antigen-presenting-cell function of interferon
gamma-treated human gingival fibroblasts.
AUTHOR: Shimabukuro Y; Murakami S; Okada H
CORPORATE SOURCE: Department of Periodontology and Endodontology, Osaka
University Faculty of Dentistry, Japan.
SOURCE: JOURNAL OF PERIODONTAL RESEARCH, (1996 Apr) 31 (3) 217-28.
Journal code: 0055107. ISSN: 0022-3484.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Dental Journals; Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19961219
Entered Medline: 19961120
AB The present study was carried out to examine the antigen-presenting cell
(APC) functions of human gingival fibroblasts (HGF) elicited with IFN
gamma. Stimulation of HGF with IFN gamma clearly induced HLA-
DR expression and enhanced expression of intercellular adhesion
molecule-1 (ICAM-1) on HGF. Despite the phenotypical resemblance of IFN
gamma-treated HGF to so-called APC, HLA-DR positive
HGF were unable to induce proliferation of allo-reactive peripheral blood
T cells (PBT) isolated from different donors. The failure of IFN
gamma-treated HGF to stimulate unprimed allo-reactive PBT was
not due to the lack of production of IL-1 or the immunosuppressive effect
of PGE2 from HGF. On the other hand, the fact that detectable expression
of CD80, ligand for CD28, was not found on IFN gamma-treated HGF may at
least in part explain the ineffective function of HGF as APC.
Interestingly, IFN gamma-treated HGF induced proliferation of primed
allo-reactive CD4+ T cells in a HLA-DR dependent
manner, suggesting that IFN gamma-treated HGF may have the ability to
stimulate pre-activated T cells. We then confirmed that high
levels of IFN gamma mRNA were detectable in inflamed gingival tissue.
Although it cannot be concluded from this study that HGF are incapable of
effectively presenting antigenic peptides to autologous T cells bearing
appropriate T cell receptors, present results suggest that HGF may be
affected by locally-secreted IFN gamma and that the IFN gamma-stimulated
HGF may play a role in regulating immune responsiveness in inflammatory
periodontal lesions.

L4 ANSWER 36 OF 79 MEDLINE
DUPLICATE 22
ACCESSION NUMBER: 96348748 MEDLINE
DOCUMENT NUMBER: 96348748 PubMed ID: 8725884
TITLE: Dual expression of human leukocyte antigen molecules and
the B7-1 costimulatory molecule (CD80) on human melanoma
cells after particle-mediated gene transfer.
AUTHOR: Albertini M R; Emler C A; Schell K; Tans K J; King D M;
Sheehy M J
CORPORATE SOURCE: University of Wisconsin Comprehensive Cancer Center,
Madison, USA.
CONTRACT NUMBER: 3-MO1-RR03186-0782 (NCRR)
CA 68466-02 (NCI)
SOURCE: CANCER GENE THERAPY, (1996 May-Jun) 3 (3) 192-201.
Journal code: 9432230. ISSN: 0929-1903.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19980206
Entered Medline: 19961108
AB The aim of this study was to determine if human melanoma cells could be
molecularly modified by particle-mediated gene transfer with a "gene gun",
using genes for interferon-gamma (IFN-gamma), the B7-1
costimulatory molecule (CD80), and human leukocyte antigen (HLA)-A2, to
augment expression of both HLA molecules and B7-1. Established and early
passage melanoma cells transfected with human IFN-gamma complementary DNA
(cDNA) produced IFN-gamma (50-5,000 pg/mL). The biological effect of this
IFN-gamma transgene included an upregulation, or de novo appearance, of
HLA expression. These melanoma cells had no detectable baseline surface
expression of the B7-1 costimulatory molecule, but 8% to 31% of these
cells became B7-1 positive with no selection procedure after gene transfer
with human B7-1 cDNA. After combination gene transfer with cDNAs for both
IFN-gamma and B7-1, 9% to 33% of these cells expressed both HLA-
DR and B7-1. In combination gene transfer experiments with cDNAs
for both HLA-A2 and B7-1, dual expression of HLA-A2 and B7-1 was achieved
in 10% to 17% of the melanoma cells. Thus, the molecular modification of
human melanoma cells to increase expression of both HLA and B7-1 can be

achieved by particle-mediated gene delivery and presents a promising
strategy to stimulate antimelanoma T-cell immunity. Key words:
Melanoma; T cells; B7-1 costimulatory molecule (CD80); major
histocompatibility complex.

L4 ANSWER 37 OF 79 MEDLINE
DUPLICATE 23
ACCESSION NUMBER: 97177474 MEDLINE
DOCUMENT NUMBER: 97177474 PubMed ID: 9024990
TITLE: Synergistic effect of prolactin on IFN-gamma-mediated
growth arrest in human monoblastic cells: correlation with
the up-regulation of IFN-gamma receptor gene expression.
AUTHOR: Sedo A; Van Weyenbergh J; Rouillard D; Bauvois B
CORPORATE SOURCE: Unite 365 INSERM Institut Curie, Paris, France.
SOURCE: IMMUNOLOGY LETTERS, (1996 Nov) 53 (2-3) 125-30.
Journal code: 7910006. ISSN: 0165-2478.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970523
Last Updated on STN: 19970523
Entered Medline: 19970512
AB Interferon-gamma (IFN-gamma) stimulates the
development of monocytic features in human myeloid precursors. Because
transcriptional regulation of IFN-gamma and the pituitary hormone
prolactin (PRL) has been described to involve common Jak-STAT pathways, we
addressed here the question of whether PRL plays a role in monoblastic
(U937) cell growth and macrophage maturation. In contrast to IFN-gamma,
PRL did not affect U937 cell growth nor induction of differentiation as
assessed by the unchanged cell surface expression of maturation markers
CD11b and HLA-DR class II. However, PRL in synergy
with IFN-gamma inhibited, in a time- and dose-dependence, proliferation of
U937 cells without influencing their maturation induced by IFN-gamma.
IFN-gamma and PRL both affected the expression of the IFN-gamma receptor
(IFN-gamma R) gene by increasing IFN-gamma R mRNA levels. The rise in
IFN-gamma R transcripts was accompanied by a low but significant release
of IL-6 which has previously been shown to stabilize IFN-gamma R mRNA.
Moreover, a transient increase in surface expression of IFN-gamma R was
observed in U937 cells treated by IFN-gamma alone or in combination with
PRL, whereas no apparent modulation of cell surface IFN-gamma R was
observed in cells treated with PRL. Lastly, PRL did not induce
transcriptional activation in IFN-gamma inducible IRF-1 and Fc gamma RI
genes in U937 cells. Together, our data indicate that IL-6 secretion and
increased expression of the IFN-gamma R gene correlate with U937 cell
growth arrest induced by IFN-gamma and PRL, probably through a signaling
mechanism which does not involve the Stat 1/IRF-1 pathway.

L4 ANSWER 38 OF 79 MEDLINE
DUPLICATE 24
ACCESSION NUMBER: 96145220 MEDLINE
DOCUMENT NUMBER: 96145220 PubMed ID: 8558915
TITLE: Interleukin 4 and interferon gamma costimulate the expansion of early human myeloid
colony-forming cells. Proposal of a model for the
regulation of myelopoiesis by interleukin 4 and
interferon gamma and its integration with the regulation of the immune response.
AUTHOR: Snoeck H W; Lenjou M; Nys G; Lardon F; Peetermans M E; Van
Bockstaele D R; Moulijn A; Haenen L; Berneman Z N
CORPORATE SOURCE: Laboratory of Experimental Hematology, University of
Antwerp (UIA), Belgium.
SOURCE: LEUKEMIA, (1996 Jan) 10 (1) 117-22.
Journal code: 8704895. ISSN: 0887-6924.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199602
ENTRY DATE: Entered STN: 19960312
Last Updated on STN: 19960312
Entered Medline: 19960226
AB We have previously shown that interleukin 4 (IL-4) and interferon
gamma (INF-gamma) reciprocally regulate the production of
granulocytes and monocytes from mature monopotential hematopoietic
progenitor cells, while at the level of the very primitive stem cells
IFN-gamma is a selective inhibitor of proliferation and differentiation,
and IL-4 has weak stimulatory effects. We investigated the effects of IL-4
and IFN-gamma on the expansion in suspension culture of myeloid
colony-forming cells (CFCs) induced by either IL-3 or IL-1+IL-3, using on
the one hand more differentiated CD34+HLA-DR strongly
positive (HLA-DR++) and on the other hand more primitive Cd34+HLA-DR weakly positive (HLA-DR+/-) human bone marrow cells. It is shown that both IL-4 and
IFN-gamma stimulate the IL-3- and IL-3+IL-1-induced expansion of

the number of CFCs in the HLA-DR+/- population. In the
presence, but not in the absence of IL-1, additive effects of IL-4 and
IFN-gamma were seen. We could not demonstrate any IL-3-like effect by IL-4
on early human hematopoietic progenitors. No expansion of CFC number was
seen in the HLA-DR++ population. Based on these data
and on data which we have published previously, a model for the regulation
of myelopoiesis by IL-4 and IFN-gamma is proposed. In this model, IL-4 and
IFN-gamma, which are both immune recognition induced inflammatory
cytokines, both stimulate the expansion and recruitment of early
myeloid progenitors, whereas at the level of their terminal
differentiation, the balance between both cytokines determines whether
preferentially monocytes/macrophages (IFN-gamma) or granulocytes (IL-4)
are being produced. At the level of the most primitive cells, the
inhibitory action of IFN-gamma might prevent differentiative exhaustion of
the stem cell compartment in situations of hematopoietic stress.

L4 ANSWER 39 OF 79 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:332173 CAPLUS
DOCUMENT NUMBER: 125:7867
TITLE: IFN-.gamma.-stimulated enhancement of MHC class II
antigen expression by the human mast cell line HMC-1
AUTHOR(S): Love, Kelley S.; Lakshmanan, Romola R.; Butterfield,
Joseph H.; Fox, Charity C.
CORPORATE SOURCE: Dep. of Medical Microbiology and Immunology and
Internal Medicine, Ohio State Univ. College of
Medicine, Columbus, OH, 43210, USA
SOURCE: Cellular Immunology (1996), 170(1), 85-90
CODEN: CLIMB8; ISSN: 0008-8749
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The expression of MHC class II mols. by human mast cells has been reported
in immunohistochem. surveys of inflammatory conditions, such as in
tuberculin hypersensitivity. While these data suggest that human mast
cells may act as antigen-presenting cells under inflammatory conditions,
the induction of class II antigens on human mast cells has not been examd.
In this study, we detd. the effects of the inflammatory cytokines
IFN-.gamma. and IL-4 on the expression of class II antigens HLA-DR, -DP,
and -DQ by the human mast cell line HMC-1. HMC-1 cells were incubated
with or without 1000 U/mL recombinant human IFN-.gamma. Z(rhIFN-.gamma.)
and IL-4 (rhIL-4) for 72 h and analyzed for expression of MHC class II
antigens by direct immunofluorescence and flow cytometry. HMC-1 cells
expressed significant levels of HLA-DR and moderate levels of HLA-DP and
-DQ at baseline and when cultured without exogenous cytokines.
Stimulation by rhIFN-.gamma. for 72 h significantly increased the levels
of HLA-DR and -DP expression but did not affect levels of HLA-DQ.
Stimulation by rhIL-4 for 72 h had minimal effect on expression of class
II mols., but induced a significant difference in levels of ICAM-1 (CD54)
expression, indicating that this cytokine is involved instead in the
control of certain accessory mols. Our data showing constitutive
expression of MHC class II mols. on HMC-1 cells and upregulation of that
expression by rhIFN-.gamma. suggest that human mast cells function as
antigen-presenting cells at sites where inflammatory cytokines are
present.

L4 ANSWER 40 OF 79 MEDLINE
DUPLICATE 25
ACCESSION NUMBER: 96404648 MEDLINE
DOCUMENT NUMBER: 96404648 PubMed ID: 8808789
TITLE: IL-10 production by adult human derived microglial cells.
AUTHOR: Williams K; Dooley N; Ulvestad E; Becher B; Antel J P
CORPORATE SOURCE: Department of Pathology, Dartmouth Medical School,
Dartmouth-Hitchcock Medical Center, Lebanon, NH 03756, USA.
CONTRACT NUMBER: T32 AI 07363 (NIAID)
SOURCE: NEUROCHEMISTRY INTERNATIONAL, (1996 Jul) 29 (1) 55-64.
Journal code: 8006959. ISSN: 0197-0186.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961204
AB Microglia, a population of central nervous system (CNS) macrophages, have
been demonstrated to support immune accessory and effector functions in
the CNS. Numerous studies support the role of microglia in CNS development
and pathology, where activation of microglia is consistently noted. The
current study investigated microglial immune functions under basal and
activation conditions and assessed the ability of interleukin-10 (IL-10),
added exogenously or produced by microglia, to down-regulate microglial

functions. This report demonstrates that microglia from the adult human
brain produce IL-10 following interferon-gamma /lipopolysaccharide activation. Functionally, recombinant human IL-10
down-regulated basal HLA-DR expression by microglia
and inhibited, in a dose-dependent response, the ability of microglia to
stimulate CD4+ T-cells in antigen presentation assays. These data,
together with recent observations of the inhibition of experimental
allergic encephalomyelitis (EAE) following IL-10 administration and
reduced CNS infection by Listeria monocytogenes after anti-IL-10
treatment, suggest that IL-10 production by microglia may have important
immune-regulatory functions in CNS disease and disease models.

L4 ANSWER 41 OF 79 CANCERLIT
ACCESSION NUMBER: 96602227 CANCERLIT
DOCUMENT NUMBER: 96602227
TITLE: Gene therapy of human melanoma by particle bombardment
(Meeting abstract).
AUTHOR: Albertini M R; Sheehy M J; Schell K; Emler C; Tans K; King
D
CORPORATE SOURCE: University of Wisconsin Comprehensive Cancer Center,
Madison, WI 53792.
SOURCE: Proc Annu Meet Am Assoc Cancer Res, (1995) 36 A2934.
ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACTS)
LANGUAGE: English
FILE SEGMENT: Institute for Cell and Developmental Biology
ENTRY MONTH: 199604
ENTRY DATE: Entered STN: 19970509
Last Updated on STN: 19970509
AB While progress has been made understanding the essential components
required for effective T-cell recognition of human melanoma, this disease
remains incurable once metastatic. This project utilizes particle-mediated
gene transfer (PMGT) to deliver distinct genes to melanoma cells to
stimulate anti-melanoma T-cell immunity. The necessary components
for effective T-cell recognition include (1) a peptide antigen
preferentially expressed in melanoma, (2) appropriate major
histocompatibility (MHC) expression for presentation of the peptide and
(3) co-stimulatory molecule expression. Established and early-passage
human melanoma cell lines were bombarded with gold beads coated with human
interferon-gamma (IFN-y) cDNA. These transfected
melanoma cell lines produced IFN-y (28.8 pg/ml to 167.9 pg/ml) when
evaluated 24, 48, and 72 hr following PMGT. The biologic effect of this
IFN-y transgene included an upregulation of MHC class I expression and
dramatic upregulation of MHC class II expression for HLA-DP and
HLA-DR but not for HLA-DQ. These melanoma cell lines had
no detectable surface expression of the B7-1 co-stimulatory molecule when
evaluated by flow cytometry with the BB1 monoclonal antibody. Following
PMGT with the human B7-1 cDNA, approximately 6% of the M-21 melanoma cells
had detectable surface expression for B7-1. Ongoing experiments are aimed
at enhancing the gene transfer efficiency as well as determining the in
vitro immunogenicity of these IFN-y and B7-1 transfected cells. The
molecular modification of human melanoma cells can be successfully
achieved by PMGT with the cDNAs for IFN-y and for the B7-1 co-stimulatory
molecule and presents a promising strategy to stimulate
antimelanoma T-cell immunity.

L4 ANSWER 42 OF 79 MEDLINE
DUPLICATE 26
ACCESSION NUMBER: 96418518 MEDLINE
DOCUMENT NUMBER: 96418518 PubMed ID: 8821303
TITLE: Upregulation of IgE synthesis by staphylococcal toxic shock
syndrome toxin-1 in peripheral blood mononuclear cells from
patients with atopic dermatitis.
AUTHOR: Hofer M F; Lester M R; Schlievert P M; Leung D Y
CORPORATE SOURCE: Department of Paediatrics, National Jewish Center for
Immunology and Respiratory Medicine, Denver, CO 80206, USA.
CONTRACT NUMBER: AR-41256 (NIAMS)
HL-37260 (NHLBI)
RR-00051 (NCRR)
+
SOURCE: CLINICAL AND EXPERIMENTAL ALLERGY, (1995 Dec) 25 (12)
1218-27.
Journal code: 8906443. ISSN: 0954-7894.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19961219
Entered Medline: 19961105
AB BACKGROUND: Atopic dermatitis (AD) is a chronic skin disease associated
with increased IgE synthesis and colonization with Staphylococcus aureus
secreting exotoxins, such as Toxic Shock Syndrome Toxin-1 (TSST-1).
OBJECTIVES: In this study, we were interested in determining the in vitro
effects of TSST-1 on IgE synthesis in peripheral blood mononuclear cells

from patients with AD. METHODS: We stimulated peripheral blood mononuclear cells (PBMC) from AD patients with a wide range of TSST-1 concentrations and measured IgE synthesis by enzyme-linked immunosorbent assay (ELISA) after 14 days. RESULTS: We show herein that TSST-1 produced antagonistic effects on IgE synthesis by PBMC from AD patients, depending on the concentration used: IgE synthesis was inhibited at 1000 pg/mL ($P < 0.05$) and enhanced at 0.01 pg/mL ($P < 0.01$) of toxin. TSST-1 was found to induce the production of much higher amounts of interferon-gamma (IFN gamma) at 1000 pg/mL than at 0.01 pg/mL of toxin ($P = 0.0001$). More importantly, immunoglobulin E (IgE) synthesis was enhanced by TSST-1 at 1 pg/mL in the presence of antibodies blocking IFN gamma activity. The other immunoglobulin (Ig) isotypes were also increased after TSST-1 stimulation suggesting that the enhanced IgE synthesis was secondary to a polyclonal B cell activation rather than an isotype switch. TSST-1-stimulated IgE synthesis was T cell-dependent because purified tonsil B cells were only able to synthesize increased amounts of IgE when small numbers of T cells were added to the cultures. Anti-HLA-DR and anti-LFA-1 monoclonal antibodies (MoAb) inhibited TSST-1-enhanced IgE synthesis, suggesting that the bridging of the T cell receptor (TCR) and major histocompatibility complex (MHC) class II on B cells was necessary for activation of B cell differentiation. CONCLUSION: These data indicate that staphylococcal superantigens are able, at concentrations inducing low amounts of IFN gamma, to stimulate IgE synthesis by PBMC from AD patients, and suggest that staphylococcal toxins may contribute to elevated IgE synthesis in AD.

L4 ANSWER 43 OF 79 MEDLINE
DUPLICATE 27
ACCESSION NUMBER: 96093889 MEDLINE
DOCUMENT NUMBER: 96093889 PubMed ID: 7576910
TITLE: HIV type 1 grown on interferon gamma -treated U937 cells shows selective increase in virion-associated intercellular adhesion molecule 1 and HLA-DR and enhanced infectivity for CD4-negative cells.
AUTHOR: Castilletti C; Capobianchi M R; Fais S; Abbate I; Ficociello B; Ameglio F; Cordiali Fei P; Santini S M; Dianzani F
CORPORATE SOURCE: Institute of Virology, University La Sapienza, Rome.
SOURCE: AIDS RESEARCH AND HUMAN RETROVIRUSES, (1995 May) 11 (5) 547-53.
Journal code: 8709376. ISSN: 0889-2229.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 19970203
Entered Medline: 19951219
AB Cellular adhesion molecules, such as ICAM-1, -2, and -3; LFA-1; and HLA class I and II are incorporated into HIV-1 virions during budding from infected cells. These virion-associated molecules can be involved in the adsorption to susceptible cells displaying the corresponding counterligands. A number of cytokines have been shown to upregulate the cellular expression of adhesion molecules, such as ICAM-1 and HLA-DR. In this study we investigated the effects of IFN-gamma on the incorporation of ICAM-1, LFA-1, and HLA-DR into mature HIV-1 progeny from chronically infected cells. The ability of such virus progeny to infect either CD4-positive or -negative cells was also investigated. The results indicate that IFN-gamma stimulates the expression of ICAM-1 and of HLA-DR on HIV-1-infected cells, whereas LFA-1 expression is unaffected. The same modifications were also observed on virus progeny, because specific MAbs to ICAM-1 and HLA-DR captured infectious HIV-1 from IFN-treated cells with higher efficiency as compared to virus from control cells, whereas virus binding to anti LFA-1 MAb was unchanged. Moreover, the HIV-1 progeny released from IFN-treated cells showed an increased ability to bind to and to infect CD4-negative cells, whereas the infectivity was basically unchanged for CD4-positive cells. Our results suggest that cytokines, as well as other soluble factors, may expand the host cell range of HIV-1, possibly through modifications of the cell-derived surface molecules on the virions.(ABSTRACT TRUNCATED AT 250 WORDS)

L4 ANSWER 44 OF 79 MEDLINE
DUPLICATE 28
ACCESSION NUMBER: 95268072 MEDLINE
DOCUMENT NUMBER: 95268072 PubMed ID: 7749123
TITLE: Immune responses by cord blood cells.
AUTHOR: Roncarolo M G; Bigler M; Ciuti E; Martino S; Tovo P A
CORPORATE SOURCE: DNAX Research Institute, Human Immunology Department, Palo

Alto, CA 94304-1104, USA.
SOURCE: BLOOD CELLS, (1994) 20 (2-3) 573-85; discussion 585-6.
Journal code: 7513567. ISSN: 0340-4684.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950629
Last Updated on STN: 19950629
Entered Medline: 19950620

AB In the present study, the biological properties of cord blood cells were investigated. Cord blood mononuclear cells and T cells responded normally to activation by alloantigens in primary mixed leukocyte reactions (MLRs), indicating that cord blood T cells can be normally activated via their TcR and have normal proliferative capacities. In addition, they expressed normal levels of accessory molecules such as CD28 and LFA-1, which contribute to amplify their responses. In contrast, cord blood mononuclear cells, but not cord blood monocytes, had a reduced capacity to stimulate allogeneic cells in primary MLRs. In addition, cord blood monocytes express lower levels of HLA-DR and ICAM-1 compared to adult peripheral blood monocytes. Cord blood mononuclear cells were also impaired in their capacity to generate allogeneic cytotoxic activity in primary mixed leukocyte cultures (MLCs). In contrast, cord blood B cells were similar to adult B cells in their capacity to switch to immunoglobulin E producing cells when incubated with interleukin-4 (IL-4) and anti-CD40 monoclonal antibody. We also demonstrated that IL-2, IL-6, and tumor necrosis factor-alpha (TNF-alpha) production by activated cord blood mononuclear cells was comparable to that observed with peripheral blood mononuclear cells isolated from normal adult donors. In contrast, interferon-gamma (IFN-gamma) was significantly decreased, whereas IL-4 and IL-5 were absent. Granulocyte-macrophage colony-stimulating factor (GM-CSF) levels were in general higher in the supernatants of cord blood cells. Thus, cord blood immune responses differ from those of peripheral blood at several levels. Whether these differences account for a reduced capacity of transplanted cord blood cells to modulate graft vs. host disease remains to be determined.

L4 ANSWER 45 OF 79 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:104975 CAPLUS
DOCUMENT NUMBER: 120:104975
TITLE: Increased proliferation, cytotoxicity, and gene expression after stimulation of human peripheral blood T lymphocytes through a surface ganglioside (GD3)
AUTHOR(S): Norihisa, Yoko; McVicar, Daniel W.; Ghosh, Paritosh; Houghton, Alan N.; Longo, Dan L.; Creekmore, Stephen P.; Blake, Trevor; Ortaldo, John R.; Young, Howard A.
CORPORATE SOURCE: Frederick Cancer Res. Dev. Cent., Natl. Cancer Inst., Frederick, MD, 21702-1201, USA
SOURCE: Journal of Immunology (1994), 152(2), 485-95
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous studies have suggested that gangliosides have an important role in cell signaling and recognition. However, their specific function in these processes has not been clearly defined. A mAb, R24, that reacts specifically with a cell surface ganglioside (GD3) has been demonstrated to stimulate proliferation of T cells derived from human peripheral blood. In this study, the authors have investigated the mechanisms by which the R24 mAb affects T cell functions. The authors have obsd. that the R24 mAb stimulates GD3+ T cell proliferation, cytotoxicity, and surface marker expression of IL-2R .alpha.-chain, IL-2R .beta.-chain, HLA -DR, CD11a, and CD11c. Addnl., IFN-.gamma. activity but not IL-1, IL-2, or IL-4 activity was present in culture supernatants 72 h after R24 stimulation. In some donors, increased IL-6 and TNF-.alpha. activity also was detected after R24 treatment. Furthermore, R24 treatment resulted in translocation of c-rel, but little or no NF.kappa.B p50 or p65, from the cytoplasm to the nucleus and an increase of NF.kappa.B binding complexes contg. c-rel and p50. This treatment also caused increased tyrosine phosphorylation of specific protein substrates. R24-stimulated increases in proliferation, cytotoxicity, and cell surface protein expression could be blocked by cyclosporin and staurosporine, indicating that cyclophilin/calcineurin and protein kinase C may be involved in the R24 signaling pathway. Addnl., herbimycin A, a tyrosine kinase inhibitor, blocked the R24-stimulated increase in proliferation but not cytotoxicity at concns. consistent with specificity for tyrosine kinases. Thus, multiple biochem. pathways are involved in the activation of human T cells by R24.

L4 ANSWER 46 OF 79 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:382310 CAPLUS
DOCUMENT NUMBER: 125:84534
TITLE: Regulatory mechanism of IFN-.gamma.-induced expression of HLA class II antigen
AUTHOR(S): Koide, Yukio; Ryu, Keiko; Nezu, Nobukazu; Yoshida, Takato
CORPORATE SOURCE: Dep. Microbiol., Hamamatsu Univ. Sch. Medicine, Hamamatsue, Japan
SOURCE: MHC, Major Histocompatibility Complex (1994), 1(1), 27-28
CODEN: MMHCFQ
PUBLISHER: Nippon Soshiki Tekigosei Gakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB .gamma. Interferon increased the level of antigen HLA-DR mRNA, i.e. stimulates antigen HLA-DR expression, in T98G cells. The stimulation is inhibited by tyrosine kinase inhibitor: genistein, herbimycin and tyrphostin.

L4 ANSWER 47 OF 79 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:601498 CAPLUS
DOCUMENT NUMBER: 119:201498
TITLE: Enhanced expression of HLA molecules and stimulation of autologous human tumor infiltrating lymphocytes following transduction of melanoma cells with .gamma.-interferon genes
AUTHOR(S): Ogasawara, Masahiro; Rosenberg, Steven A.
CORPORATE SOURCE: Surg. Branch, Natl. Cancer Inst., Bethesda, MD, 20892, USA
SOURCE: Cancer Research (1993), 53(15), 3561-8
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Gene therapy for cancer is being tested in clin. trials using tumor-infiltrating lymphocytes (TIL) or tumor cells modified by the insertion of genes coding for interleukin 2 or tumor necrosis factor .alpha.. In the present study, the authors investigated the feasibility of transducing human tumor cells with genes coding for .gamma.-interferon (IFN.gamma.) or .alpha.-interferon (IFN.alpha.), which are two other cytokines that can enhance host antitumor immune responses. Tumor cells from 12 melanoma and 2 renal cell carcinoma patients were transduced with retroviral vectors contg. the gene for IFN.gamma.. Northern blot anal. showed IFN.gamma. transcription only in the IFN.gamma. gene-transduced cells. In both IFN.gamma.-secreting and non-secreting tumor lines, the cell surface expression of HLA class I and class II mols. increased following transduction. However, the magnitude of the increase in HLA expression appeared to be greater in tumor lines secreting IFN.gamma.. Two melanoma cell lines were successfully transduced with an IFN.alpha. retroviral vector. Melanoma cells transduced with the IFN.alpha. gene contained IFN.alpha. RNA transcripts and secreted large amts. of IFN.alpha.. In contrast to cells transduced with the IFN.gamma. gene, the expression of HLA class II mols. was not increased in the IFN.alpha. gene-transduced cells. Finally, the authors tested the ability of HLA.Dr+ melanoma cells, which had been transduced with the IFN.gamma. gene, to stimulate specific cytokine release by autologous CD4+ TIL. Specific secretion of cytokine by TIL occurred when the TIL and IFN.gamma. gene-transduced tumor cells were cultured together but not when TIL were cultured alone or with control nontransduced tumor cells. These results suggest that mols. newly expressed on the transduced cells promoted antigen presentation and T-cell responses against the transduced tumor cells. The insertion of the IFN.gamma. gene into melanoma cells may be useful either for active immunization against melanoma or for the generation of TIL to be used in adoptive immunotherapy.

L4 ANSWER 48 OF 79 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:225273 BIOSIS
DOCUMENT NUMBER: PREV199395116448
TITLE: Accessory cell function of human eosinophils: HLA-DR-dependent, MHC-restricted antigen-presentation and IL-1-alpha expression.
AUTHOR(S): Weller, Peter F. (1); Rand, Thomas H.; Barrett, Tonya; Elovic, Aram; Wong, David T. W.; Finberg, Robert W.
CORPORATE SOURCE: (1) Beth Israel Hosp., DA-617, 330 Brookline Ave., Boston, MA 02215
SOURCE: Journal of Immunology, (1993) Vol. 150, No. 6, pp. 2554-2562.
ISSN: 0022-1767.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Although peripheral blood eosinophils express little of the class II MHC protein, HLA-DR, eosinophils could be induced to express HLA-DR by exposures to cytokines, including

granulocyte-macrophage-CSF, IL-4, and IFN-gamma, with granulocyte-
macrophage-CSF eliciting the greatest level of HLA-DR
expression as assessed by flow cytometry. The capacity of HLA-
DR+ eosinophils to function as APC was evaluated with blood
eosinophils isolated free of mononuclear cells, cultured with
granulocyte-macrophage-CSF to induce HLA-DR expression
and then exposed to the Ag tetanus toxoid. HLA-DR+
eosinophils fixed with paraformaldehyde after Ag exposure stimulated T
cell proliferation, whereas HLA-DR+ eosinophils fixed
with paraformaldehyde before Ag exposure failed to stimulate
lymphocyte proliferation. The lymphocyte proliferative responses elicited
by Ag-pulsed HLA-DR+ eosinophils were inhibited by
anti-HLA-DR mAb and were restricted to HLA-
DR compatible lymphocytes. Moreover, eosinophils from a
hypereosinophilic donor, both before and more prominently after
stimulation with PMA, contained transcripts for IL-1-alpha mRNA detectable
by Northern blot hybridization and in situ hybridization and expressed
IL-1-alpha protein detectable by immunohistochemistry. These findings
indicate that human eosinophils can process Ag, express the costimulatory
cytokine IL-1-alpha, and after cytokine-elicited induction of HLA
-DR expression can function as HLA-DR
-dependent, MHC-restricted APC in stimulating T lymphocyte responses.

L4 ANSWER 49 OF 79 MEDLINE
DUPLICATE 29
ACCESSION NUMBER: 93314692 MEDLINE
DOCUMENT NUMBER: 93314692 PubMed ID: 8100773
TITLE: Activation with superantigens induces programmed death in
antigen-primed CD4+ class II+ major histocompatibility
complex T lymphocytes via a CD11a/CD18-dependent mechanism.
AUTHOR: Damle N K; Leytze G; Klussman K; Ledbetter J A
CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research Institute,
Seattle.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1993 Jul) 23 (7) 1513-22.
Journal code: 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 19930820
Last Updated on STN: 19950206
Entered Medline: 19930809

AB Staphylococcal enterotoxin superantigens (SAg) bind class II major
histocompatibility complex (MHC) molecules on antigen-presenting cells
(APC) and upon cell-to-cell contact stimulate proliferation of T
cells expressing appropriate V beta gene products. In addition, SAg can
also deliver negative signals to Ag-specific T cells resulting in a state
of unresponsiveness or a loss of viability. The present study examines the
functional consequences of a direct interaction of SAg with
alloAg-specific class II MHC+ CD4+ T cell lines (TCL). Our results
demonstrate that SAg induce programmed death (apoptosis) in a majority of
Ag-specific CD4+ T cells accompanied by genomic DNA fragmentation. SAg
binding to Ag-specific TCL resulted in a rapid mobilization of
intracellular free calcium ([Ca2+]i) and transcription of a number of
cytokine genes including interleukin-2(IL-2), IL-4, interferon-
gamma (IFN-gamma), granulocyte-macrophage colony-stimulating
factor (GM-CSF), and granzyme B indicating the activation of primed T
cells. Both SAg-induced cytokine gene expression as well as subsequent
death were significantly inhibited by a tyrosine kinase inhibitor
herbimycin A and also by cyclosporin A. SAg-induced death of primed T
cells was also inhibited by monoclonal antibodies (mAb) directed at the
CD11a/CD18 molecule but not those reactive with other T cell surface
molecules such as CD2, CD7, CD28, CD29 or CD49d. None of these mAb,
including anti-CD11a/CD18, had any effect on SAg-induced expression of
IL-2 and IL-4 genes or SAg-induced [Ca2+]i response. Addition of cytokines
such as IL-1 alpha, IL-2, IL-4, IL-6, GM-CSF, IFN-gamma, tumor necrosis
factor (TNF-alpha, or TNF-beta), or neutralizing Ab to these cytokines had
no effect on SAg-induced death of Ag-specific TCL. The T cells which
survived the death-inducing effects of SAg showed down-regulation of the
CD3/T cell receptor and up-regulation of CD2 and HLA-DR
expression, and upon re-exposure to the same SAg upregulated expression of
mRNA for IL-2 and IFN-gamma. Presentation of SAg by B7+ ICAM-1+ LFA-3+ DR+
professional APC was also able to induce the death of Ag-specific TCL.
Together these results suggest that the activation with SAg causes
programmed death of Ag-specific TCL cells via a mechanism that requires
late participation of the CD11a/CD18 molecule.

L4 ANSWER 50 OF 79 MEDLINE
DUPLICATE 30
ACCESSION NUMBER: 94061888 MEDLINE
DOCUMENT NUMBER: 94061888 PubMed ID: 8242663
TITLE: Interleukin-4 plus tumor necrosis factor alpha augments the
antigenicity of melanoma cells.
AUTHOR: Hoon D S; Hayashi Y; Morisaki T; Foshag L J; Morton D L
CORPORATE SOURCE: John Wayne Cancer Institute, Saint John's Hospital and
Health Center, Santa Monica, CA 90404.
CONTRACT NUMBER: CA 12582 (NCI)
SOURCE: CANCER IMMUNOLOGY, IMMUNOTHERAPY, (1993 Nov) 37 (6) 378-84.
Journal code: 8605732. ISSN: 0340-7004.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199401
ENTRY DATE: Entered STN: 19940201
Last Updated on STN: 19970203
Entered Medline: 19940106
AB Immune cytokines are important regulators of the immune response to
neoplastic cells. We previously reported that interleukin 4 (IL-4) and
either tumor necrosis factor alpha (TNF) or interferon
gamma (IFN) synergistically inhibit melanoma cell growth and
induce cell differentiation. In the present study we used various
combinations of IL-4, IFN and TNF to enhance the antigenicity of melanoma
cells. IL-4 plus TNF significantly increased the ability of melanoma cells
to stimulate cytotoxic T cells (CTL) and act as targets of these
CTL; IL-4 plus IFN was somewhat less effective, while TNF plus IFN was not
as effective. IL-4 plus TNF also increased the expression of HLA class I
and HLA-DR antigens on melanoma cells. The CTL lines
examined in this study were CD3+CD4+ and oligoclonal. These preclinical
results suggest that the immune response to melanoma whole-cell vaccines
might be enhanced by pretreating vaccine cells with IL-4 plus TNF.

L4 ANSWER 51 OF 79 MEDLINE
DUPLICATE 31
ACCESSION NUMBER: 93325073 MEDLINE
DOCUMENT NUMBER: 93325073 PubMed ID: 7687392
TITLE: Human CD4+ T cells proliferate to HLA-DR+ allogeneic
vascular endothelium. Identification of accessory
interactions.
AUTHOR: Savage C O; Hughes C C; McIntyre B W; Picard J K; Pober J S
CORPORATE SOURCE: Department of Vascular Biology and Section of
Transplantation Biology, Clinical Research Center, Harrow,
U.K.
CONTRACT NUMBER: HL 36028 (NHLBI)
HL 43364 (NHLBI)
SOURCE: TRANSPLANTATION, (1993 Jul) 56 (1) 128-34.
Journal code: 0132144. ISSN: 0041-1337.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 19930826
Last Updated on STN: 19960129
Entered Medline: 19930819
AB Serially passaged human endothelial cell (EC) cultures will
stimulate highly purified peripheral blood CD4+ T cells to
proliferate if and only if the EC cultures are pretreated with IFN-gamma
to induce de novo expression of MHC class II molecules, principally
HLA-DR. HLA-DR-expressing EC alone
appear sufficient to stimulate purified CD4+ T cell
proliferation without the involvement of other leukocyte populations, as
indicated by the following observations: (1) we find no contaminating
leukocytes in our EC cultures by FACS analysis or fluorescence microscopy;
specifically, there are no detectable CD45 or HLA-DR
expressing cells; (2) neither the EC cultures nor the purified CD4+ T
cells contain HLA-DR expressing cells detectable by
polymerase chain reaction (PCR) of reverse-transcribed mRNA; (3) the
stimulatory capacity of the EC cultures is maintained through serial
subculture and through low-density replating, indicating that the
stimulatory cell type must proliferate in culture as well as EC; and (4)
in contrast to MLRs, the response to EC cultures is not inhibited by
pretreatment of the stimulator cells and/or responding T cells with the
monocyte toxin L-leucine-O-methyl ester. We have used mAb to investigate
the role of various EC and T cell surface molecules in the T cell
response. mAb to HLA-DR and CD4 inhibit proliferative
responses of CD4+ T cells to EC cultures, as would be expected if T cells
recognize and proliferate to IFN-gamma-induced allogeneic class II MHC
molecules; whereas, also as expected, mAb to class I MHC molecules were
without effect. Proliferation is also inhibited by mAbs to T cell CD2 and
LFA-1 beta chain (CD18) and by mAbs to LFA-3 (CD58) and CD44, which are
expressed by T cells and EC. mAb to ICAM-1 (CD54, a ligand for LFA-1)
provides inconsistent inhibition, and mAb to ICAM-2, used with or without

anti-ICAM-1, is not inhibitory. Because both of these mAb block adhesion
of LFA-1 expressing T cells to EC, our data suggest that additional
ligands for LFA-1 must be important for allogeneic proliferation. mAb to
VLA-4 alpha or beta chains (CD49d, CD29) enhance proliferation, presumably
through direct costimulation of the T cells by these antibodies. However,
a mAb to VCAM-1, an EC ligand for VLA-4, is partially inhibitory.(ABSTRACT
TRUNCATED AT 400 WORDS)

L4 ANSWER 52 OF 79 MEDLINE
DUPLICATE 32
ACCESSION NUMBER: 93123336 MEDLINE
DOCUMENT NUMBER: 93123336 PubMed ID: 8419398
TITLE: Differential induction of stromelysin mRNA by bovine
articular chondrocytes treated with interferon-
gamma and interleukin-1 alpha.
AUTHOR: Quintavalla J C; Berg R A; Beavis A J; Piccoli S P; Rediske
J J; Kurkinen M; Patrick R A; Robertson F M
CORPORATE SOURCE: Ciba-Geigy Pharmaceuticals, Summit, New Jersey 07901.
SOURCE: JOURNAL OF CELLULAR PHYSIOLOGY, (1993 Jan) 154 (1) 113-21.
Journal code: 0050222. ISSN: 0021-9541.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199302
ENTRY DATE: Entered STN: 19930226
Last Updated on STN: 20000303
Entered Medline: 19930205
AB Articular chondrocytes from rheumatoid joints have been shown to express
class II major histocompatibility (MHC) antigens that were correlated with
the presence of interferon-gamma (IFN-gamma) in the
inflamed joint. Chondrocytes expressing MHC antigens function as antigen
presenting cells and thus stimulate lymphocyte proliferation.
These responses suggest a powerful role for the IFN-gamma stimulation of
chondrocytes. The present studies were designed to examine the functional
role of chondrocytes exposed to IFN-gamma during cartilage degradation
that occurs in synovial disease. Destruction of cartilage in arthritis is
partially attributable to metalloproteinases released by the chondrocytes
in response to interleukin-1 (IL-1). Bovine articular chondrocytes treated
with interleukin-1 alpha (IL-1 alpha) produced enhanced levels of
stromelysin mRNA, however, Northern blots could not determine the
percentage of cells responding. Exposure of bovine articular chondrocytes
to IFN-gamma induced the expression of bovine HLA-DR
(boHLA-DR) antigen in 50% of the cells. Using a modified cell sorting
technique, chondrocytes that expressed class II MHC antigens produced two
fold greater stromelysin mRNA than chondrocytes that did not express this
antigen. In contrast, collagen type II mRNA levels were similar in
chondrocytes, regardless of the expression of class II MHC antigens. In
situ hybridization studies showed that less than half of all cartilage
chondrocytes were induced to synthesize stromelysin mRNA. These
observations suggest that IFN-gamma stimulates specific
subpopulations of chondrocytes to be functionally active in
inflammation-induced metalloprotease secretion.

L4 ANSWER 53 OF 79 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:118514 BIOSIS
DOCUMENT NUMBER: PREV199395062614
TITLE: IL-10 stimulates monocytes Fc-gamma-R surface expression
and cytotoxic activity: Distinct regulation of antibody-dependent cellular cytotoxicity by IFN-gamma,IL-4,
and IL-10.
AUTHOR(S): Te Velde, Anje A.; De Waal Malefijt, Rene; Huijbens,
Richard J. F.; De Vries, Jan E.; Figdor, Carl G. (1)
CORPORATE SOURCE: (1) Div. Immunol., Neth. Cancer Inst., Plesmanlaan 121,
1066 CX Amsterdam Netherlands Antilles
SOURCE: Journal of Immunology, (1992) Vol. 149, No. 12, pp.
4048-4052.
ISSN: 0022-1767.
DOCUMENT TYPE: Article
LANGUAGE: English
AB T cell-derived cytokines IFN-gamma and IL-4 have different regulatory
effects on two functionally important molecules on human monocytes: MHC
class II Ag and the Fc receptor for monomeric IgG, Fc-gamma-RI (
CD64). MHC class II Ag, and Fc-gamma-RI are both upregulated in
the presence of IFN-gamma. IL-4 induces MHC class II Ag expression but
reduces Fc-gamma-RI expression. Recently, we showed that the cytokine
IL-10 also affects MHC class II Ag expression. Here, we demonstrate that
in contrast to the down-regulation of MHC class II Ag expression, IL-10
stimulates Fc-gamma-RI expression on human monocytes comparable to
the levels of Fc-gamma-RI expression induced by IFN-gamma. The
IL-10-induced Fc-gamma-RI expression is specific because anti-IL-10
antibodies completely reverse the IL-10-induced surface expression of

Fc-gamma-RI and correlate with an enhanced capacity to lyse anti-D-coated human rhesus-positive erythrocytes. IL-10 fails to induce the expression of Fc-gamma-RII (CD32) and Fc-gamma-RIII (CD16). Furthermore, we demonstrate that IL-10 is able to prevent down-regulation in surface membrane expression of all three Fc-gamma-R that can be found when monocytes are cultured in the presence of IL-4. In contrast to IFN-gamma, IL-10 does not restore the reduced antibody-dependent cellular cytotoxicity (ADCC) activity of IL-4-cultured monocytes. Together, these results show that, similar to IFN-gamma, IL-10 is capable of enhancing Fc-gamma-R expression and ADCC activity, and that IFN-gamma, IL-4, and IL-10 have different regulatory effects on both monocyte Ag-presenting capacity and ADCC activity.

L4 ANSWER 54 OF 79 MEDLINE
DUPLICATE 33
ACCESSION NUMBER: 92388674 MEDLINE
DOCUMENT NUMBER: 92388674 PubMed ID: 1517568
TITLE: IFN-gamma and 1,25(OH)2D3 induce on THP-1 cells distinct patterns of cell surface antigen expression, cytokine production, and responsiveness to contact with activated T cells.
AUTHOR: Vey E; Zhang J H; Dayer J M
CORPORATE SOURCE: Division of Immunology and Allergy (Hans Wilsdorf Laboratory), Hopital Cantonal Universitaire, Geneve, Switzerland.
SOURCE: JOURNAL OF IMMUNOLOGY, (1992 Sep 15) 149 (6) 2040-6. Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199210
ENTRY DATE: Entered STN: 19921023
Last Updated on STN: 19970203
Entered Medline: 19921007
AB Differentiation and maturation of monocytes are accompanied by the expression of specific surface glycoproteins, the secretion of cytokines, and the capacity to respond to ligands. These changes may be influenced by interactions with hormones, soluble lymphocytic products, or direct contact with lymphocytes. We have studied two distinct pathways in the differentiation of a human monocytic cell line, THP-1: one being induced by IFN-gamma and the other by 1 alpha,25-dihydroxyvitamin D3 (1,25(OH)2D3). In THP-1 cells, IFN-gamma induces cell surface expression of HLA-DR and CD54 and production of IL-1 beta, TNF-alpha, and IL-6. In contrast, 1,25(OH)2D3 increases cell surface expression of CD11b and CD14, but fails to stimulate cytokine production. Direct contact of THP-1 with stimulated fixed T cells markedly induces IL-1 beta, TNF-alpha, and IL-6 production by THP-1. Production is higher when THP-1 have been previously exposed to 1,25(OH)2D3 as compared to prior exposure to IFN-gamma. mAb raised against certain relevant cell surface glycoproteins on THP-1 were tested for their ability to block the response of THP-1 to T cells. Antibodies to CD11a, CD11b, and CD11c, alone or in combination, only partially blocked IL-1 beta production by THP-1, whereas antibodies to CD54 and CD14 did not. Thus other unknown structures on the THP-1 cells may be involved in the induction of THP-1 cytokine production by T cell contact.

L4 ANSWER 55 OF 79 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:20551 CAPLUS
DOCUMENT NUMBER: 118:20551
TITLE: The role of differential class II antigen expression in stimulation of allogeneic mixed lymphocyte reactions by human monocyte hybridomas
AUTHOR(S): Shaked, Abraham; Hoyos, Beatrice; Mayer, Lloyd
CORPORATE SOURCE: Dep. Surg., Mount Sinai Med. Cent., New York, NY, 10029, USA
SOURCE: Transplantation (1992), 53(6), 1341-7
CODEN: TRPLAU; ISSN: 0041-1337
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The recognition of foreign class II antigens on accessory cells is the crux of an alloreactive immune response. This phenomenon is clearly demonstrated in the primary mixed lymphocyte reaction, which correlates with the type and d. of expressed gene products of the HLA-D region. A series of human monocyte hybridomas was generated by fusing monocytes with the hypoxanthine guanine phosphoribosyl transferase (HGPRT)-deficient, HLA-D antigen-neg. U937 histiocytic cell line. Clones bearing combination of HLA-DQ, -DP with or without HLA-DR were isolated, allowing for the functional assessment of these mols. In contrast to the U937 cells, the HLA-DR+DQ+DP+ clone 16.1 could stimulate a primary allogeneic MLR. Interestingly, the DR- but DP+DQ+ clones 13 and 15 also could stimulate alloreactive T cells, and the addn. of anti-DQ or

-DP but not -DR was assocd. with significant inhibition of the MLR
response. Furthermore, .gamma.-IFN was found to have diverse effects on
class II antigen expression in the U937 cells and the hybrids.
.gamma.-IFN down-regulated the expression of HLA-DQ, -DP without altering
-DR on clone 16.1, and this was assocd. with a redn. in its MLR
stimulatory capacity. The MLR generated by this .gamma.-IFN-stimulated
hybridoma (HLA-DR+DQ-DP-) was now unaffected by the addn. of anti-DQ or
-DP mAbs. In contrast, up-regulation of DQ and DP antigens on the U937
cells by .gamma.-IFN now rendered these cells stimulatory in MLR. These
data are consistent with the concept that DQ and DP are both important
allostimulatory determinants. These results stress the potential
importance of all D-region mols. in acute allograft rejection or
successful engraftment.

L4 ANSWER 56 OF 79 MEDLINE
DUPLICATE 34
ACCESSION NUMBER: 92381704 MEDLINE
DOCUMENT NUMBER: 92381704 PubMed ID: 1380987
TITLE: Activation and differentiation of myelomonocytic cells in
rheumatoid arthritis and healthy individuals--evidence for
antagonistic in vitro regulation by interferon-
gamma and tumor necrosis factor alpha, granulocyte
monocyte colony stimulating factor and interleukin 1.
AUTHOR: Seitz M; Zwicker M; Pichler W; Gerber N
CORPORATE SOURCE: Division of Rheumatology, University Hospital, Inselspital,
Bern, Switzerland.
SOURCE: JOURNAL OF RHEUMATOLOGY, (1992 Jul) 19 (7) 1038-44.
Journal code: 7501984. ISSN: 0315-162X.
PUB. COUNTRY: Canada
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199209
ENTRY DATE: Entered STN: 19921018
Last Updated on STN: 19960129
Entered Medline: 19920925
AB We analyzed expression of HLA-DR and CD14 molecules on
myelomonocytic cells and its regulation by various inflammatory cytokines
in 6 patients with rheumatoid arthritis (RA) and 4 healthy individuals who
had undergone bone marrow aspiration. At start of the bone marrow culture
there was a significantly higher number of HLA-DR and
CD14 positive bone marrow mononuclear cells in patients with RA than in
normals. In addition, RA bone marrow mononuclear cells expressed an up to
10-fold higher mean density of both molecules than normal bone marrow
mononuclear cells during the whole culture period of up to 14 days. The
effect of the cytokines interferon-gamma (IFN-gamma),
tumor necrosis factor alpha (TNF alpha), granulocyte monocyte colony
stimulating factor (GM-CSF) and interleukin 1 (IL-1) on the expression of
CD14 or HLA-DR was different: IFN-gamma strongly
upregulated HLA-DR expression and down-regulated CD14
expression while TNF alpha, GM-CSF and IL-1 mainly stimulated CD14
expression on bone marrow mononuclear cells. Our data suggest that RA bone
marrow mononuclear cells exhibit an activated phenotype and that TNF-alpha
GM-CSF and IL-1 mainly stimulate the differentiation of bone
marrow macrophages whereas IFN-gamma activates them.

L4 ANSWER 57 OF 79 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:74817 BIOSIS
DOCUMENT NUMBER: PREV199395039317
TITLE: Cellular responses to human chondrocytes: Absence of
allogeneic responses in the presence of HLA-DR and ICAM-1.
AUTHOR(S): Jobanputra, P.; Corrigall, V.; Kingsley, G.; Panayi, G. (1)
CORPORATE SOURCE: (1) Rheumatology Unit, Div. Med., UMDS, Guy's Hosp., 4th
Floor, Hunt's House, London SE1 9RT UK
SOURCE: Clinical and Experimental Immunology, (1992) Vol. 90, No.
2, pp. 336-344.
ISSN: 0009-9104.
DOCUMENT TYPE: Article
LANGUAGE: English
AB To assess the accessory cell function of human articular chondrocytes, we
assessed the ability of human chondrocytes to stimulate
allogenic peripheral blood mononuclear cells (PBMC) and to support
phytohaemagglutinin (PHA)-induced proliferation of highly purified T
cells. We also examined the surface expression of HLA-DR
and ICAM-1 on the chondrocytes both unstimulated and stimulated with
cytokines in vitro. Chondrocytes failed to stimulate allogenic
PBMC despite the constitutive expression of MHC class I molecules and the
cytokine-induced expression of class II molecules but were able to support
T cell proliferation to PHA, IFN-gamma and to a limited extent, IL-1-beta,
induced class II expression on chondrocytes. ICAM-1 was present on 94-99%
of freshly isolated cells; this declined with culture (17-59%; P lt 0.005)

but was readily induced by IFN-gamma, IL-1-beta, and tumour necrosis
factor-alpha. Alloreactivity and, presumably, autoreactivity to .
chondrocytes requires factors in addition to the surface expression of DR
and ICAM-1. However the presence of these molecules suggests a capacity
for cell-cell interactions in inflammatory sites such as the cartilage
pannus junction.

L4 ANSWER 58 OF 79 MEDLINE
DUPLICATE 35
ACCESSION NUMBER: 92010022 MEDLINE
DOCUMENT NUMBER: 92010022 PubMed ID: 1833315
TITLE: Activation of human natural killer cells by
lipopolysaccharide and generation of interleukin-1 alpha,
beta, tumour necrosis factor and interleukin-6. Effect of
IL-1 receptor antagonist.
AUTHOR: Conti P; Dempsey R A; Reale M; Barbacane R C; Panara M R;
Bongrazio M; Mier J W
CORPORATE SOURCE: Immunology Division, School of Medicine, University of
Chieti, Italy.
SOURCE: IMMUNOLOGY, (1991 Aug) 73 (4) 450-6.
Journal code: 0374672. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199110
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19950206
Entered Medline: 19911030
AB The presence in the body of an antigen species or a bacterial
lipopolysaccharide (LPS) has a pleiotropic effect on the immune system
activating macrophages, lymphocytes and natural killer (NK) cells.
Recently it has been reported that human macrophages not only secrete
interleukin-1 (IL-1) but also its inhibitor, called IL-1 receptor
antagonist (IL-1ra), structurally similar to IL-1 beta, but with no
IL-1-like activity and which binds to the IL-1 receptor. In this study we
show that LPS stimulates NK cell activity and IL-1ra potentiates
the stimulatory effect of human recombinant interleukin-2 (hrIL-2) on NK
cell activity. In addition, we found that hrIL-1ra inhibits DNA synthesis
in lymphocyte culture stimulated with phytohaemagglutinin (PHA) (20
micrograms/ml), presumably via IL-1 inhibition. We also found that LPS is
a potent stimulator of monokines: IL-6, tumour necrosis factor-alpha
(TNF-alpha), and IL-1 beta, as determined by radioimmunoassay method, and
interferon-gamma (IFN-gamma), IL-2, TNF-alpha and IL-1
alpha, as determined by ELISA method, in peripheral blood mononuclear
cells (PBMC). We used PBMC as effector cells since LPS requires the
presence of accessory cells to activate lymphocytes and bind to the
HLA-DR molecule on accessory cells. The effect of LPS on
PBMC cytotoxicity has been compared with an endotoxin-free extract of
Escherichia coli, OM-8990, which did not provoke cytokine production nor
did it cause enhancement of NK cell activity. We found that human
recombinant IL-1ra potentiates the stimulatory effect of IL-2 on NK cell
activity, similar to hrIL-1 beta. The potentiation of IL-2 in stimulating
NK cell activity by IL-1ra is not yet understood. Since IL-1ra is a part
of the IL-1 family, it may work in a similar fashion to IL-1, which also
potentiates IL-2 to enhance NK cell activity but has been shown not to be
directly important in tumour cell killing. In addition, hrIL-1ra can
amplify the effect of IL-2 on NK activity, possibly by inhibiting the
cyclo-oxygenase products, which are immunosuppressive and are generated in
antigen-stimulated PBMC cultures. The generation of IFN-gamma by PBMC
after treatment with LPS strongly suggests that the enhancement of NK cell
activity may be indirectly due to IFN production.

L4 ANSWER 59 OF 79 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1991:159569 BIOSIS
DOCUMENT NUMBER: BA91:85369
TITLE: ALLORECOGNITION OF HLA-DR AND HLA-DQ TRANSFECTANTS BY HUMAN
CD45RA AND CD45R0 CD4 T CELLS REPERTOIRE ANALYSIS AND
ACTIVATION REQUIREMENTS.
AUTHOR(S): MERKENSCHLAGER M; IKEDA H; WILKINSON D; BEVERLY P C L;
TROWSDALE J; FISHER A G; ALTMANN D M
CORPORATE SOURCE: LABORATOIRE DE GENETIQUE MOLECULAIRE DES EUKARYOCYTES DU
CNRS, UNITE 184 DE BIOLOGIE MOLECULAIRE ET DE GENIE
GENETIQUE DE L'INSERM, FACULTE DE MEDECINE, 11 RUE HUMANN,
F-67085 STRASBOURG CEDEX, FRANCE.
SOURCE: EUR J IMMUNOL, (1991) 21 (1), 79-88.
CODEN: EJIMAF. ISSN: 0014-2980.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB We have investigated the requirements for allogeneic stimulation of human
CD4 T cells using HLA class II products expressed on various cellular

backgrounds. Human (class II-negative RJ2.2.5 mutant) B cell lines
transfected with HLA-DR or -DQ cDNA clones were efficient stimulators for highly purified CD4 T cells. HLA-
DR-transfected mouse L cells or IFN-.gamma.-induced human
fibroblasts, although able to function as accessory cells for T cell
responses to the mitogen PHA, failed to stimulate strong T cell
alloresponses. On the basis of these observations, we have employed class
II transfectants to address the following questions: (a) do CD45RA and
CD45R0 subpopulations differ in their allogeneic activation requirements.
(b) are these subpopulations skewed in their recognition of HLA-DQ vs.
HLA-DR in a manner which might support the concept that
CD45RA T cells are involved in HLA-DQ-restricted suppressor inducer
functions and (c) by using transfectants expressing individual HLA
-DR or -DQ heterodimers in combination with limiting dilution
analysis, can one for the first time obtain estimates of precursor
frequencies for allogeneic cells recognizing each of these class II
isotypes? Our results show that CD45RA and CE45R0 T cells respond
comparably to optimal numbers of stimulator cells. However, when CD45RA
and CD45R0 T cell populations depleted of endogenous accessory cells were
cultured with limiting numbers of stimulator cells, CD45R0 cells generally
responded more strongly, consistent with the elevated levels of various
adhesion molecules known to be expressed by this population. Further, we
found a similar representation of responses to HLA-DR
and -DQ antigens among populations expressing CD45RA and CD45R0 isoforms.
Finally, the precursor frequencies of allogeneic CD4 T cells responding to
particular HLA-DR alleles were higher than to -DQ,
only by a factor of about 1.6, indicating that HLA-DQ recognition may
occur more frequently than implied from previous antibody blocking
studies.

L4 ANSWER 60 OF 79 MEDLINE
DUPLICATE 36
ACCESSION NUMBER: 90352394 MEDLINE
DOCUMENT NUMBER: 90352394 PubMed ID: 2117474
TITLE: Interferon gamma encapsulated into liposomes enhances the activity of monocytes and natural
killer cells and has antiproliferative effects on tumor
cells in vitro.
AUTHOR: Rutenfranz I; Bauer A; Kirchner H
CORPORATE SOURCE: Institute of Immunology and Transfusion Medicine,
University of Lubeck, Federal Republic of Germany.
SOURCE: BLUT, (1990 Jul) 61 (1) 30-7.
Journal code: 0173401. ISSN: 0006-5242.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199009
ENTRY DATE: Entered STN: 19901026
Last Updated on STN: 19970203
Entered Medline: 19900924
AB The effects of human interferon gamma (IFN gamma)
encapsulated into liposomes were investigated in vitro. Monocytes were
induced to release a cytotoxic factor with either IFN gamma encapsulated
into liposomes, free IFN gamma or lipopolysaccharide (LPS). If IFN gamma
was applied in the liposomal form, less IFN activity was required to
stimulate monocytes. Most of the cytotoxic factor was secreted
during the first 4 h of stimulation. The cytotoxic factor in supernatants
from PMNLs was completely neutralized by a monospecific polyclonal
antiserum to tumor necrosis factor (TNF). Combining subthreshold doses of
IFN gamma liposomes or IFN gamma with lipopolysaccharide synergistically
enhanced the release of TNF. In fluorescence analysis, altered expression
of the class II HLA-DR antigen on LeuM3 positive
monocytes was induced with IFN gamma liposomes as well as with IFN gamma.
Not only monocytes but also natural killer (NK) cells were stimulated to
higher cytotoxicity by IFN gamma liposomes in a dose-dependent manner. In
comparison with IFN gamma, the same amount of activity was necessary for
adequate stimulation of NK-cells against the K562 target cells.
Furthermore, the antiproliferative effects of IFN gamma liposomes and free
IFN gamma on several human tumor cell lines was compared. Among several
cell lines tested, U937 and A549 turned out to be sensitive to IFN gamma,
and both cell lines reacted with 50% growth inhibition at a lower amount
of gamma presented by liposomes than in the free form. These data show
production of IFN gamma liposomes which possess immunomodulatory and
antiproliferative activity in vitro. In several of the test systems
studied, liposome-encapsulated IFN gamma was more effective than free IFN
gamma.

L4 ANSWER 61 OF 79 MEDLINE
DUPLICATE 37
ACCESSION NUMBER: 89093934 MEDLINE
DOCUMENT NUMBER: 89093934 PubMed ID: 2492049

TITLE: Regulation of monocyte/macrophage C2 production and HLA-DR
expression by IL-4 (BSF-1) and IFN-gamma.
AUTHOR: Littman B H; Dastvan F F; Carlson P L; Sanders K M
CORPORATE SOURCE: Rheumatology Section, McGuire V.A. Medical Center,
Richmond, VA 23249.
SOURCE: JOURNAL OF IMMUNOLOGY, (1989 Jan 15) 142 (2) 520-5.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198902
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19890214

AB IL-4 was originally described on the basis of its ability to co-
stimulate the proliferation of resting B cells treated with
anti-IgM. Recently, this cytokine has been shown to have other effects on
mast cells, T cells, B cells, and macrophages. We studied the ability of
IL-4 to regulate the production of C2 by human monocytes and monocytic
cell lines and compared this with stimulation of HLA-DR
expression, another recently described activity of IL-4. Responses to IL-4
were compared to IFN-gamma, a cytokine with both activities. IL-4
up-regulated C2 production by human monocytes and this effect was not
inhibited by neutralizing anti-IFN-gamma antibody. IL-4 also stimulated C2
production by HL-60 cells that had been pre-treated with vitamin D3 to
induce monocytic differentiation. IL-4 did not stimulate C2
production by U937 cells. IFN-gamma, in contrast to IL-4,
stimulates C2 production by all three cell types. Although IL-4
increased C2 production by HL-60 cells we could not detect C2 mRNA by
Northern blotting. However, co-stimulation of these cells with IL-4 and
low concentrations of IFN-gamma resulted in an additive effect on C2
production and a greater increase in C2 mRNA than was seen with IFN-gamma
alone. As reported by others, IL-4-stimulated HLA-DR
expression by monocytes. In contrast to our findings regarding C2
production, stimulation of HLA-DR expression was
inhibited by neutralizing anti-IFN-gamma mAb and IL-4 did not
stimulate HLA-DR expression by U937 or HL-60
cells. IFN-gamma stimulated HLA-DR expression by all
three cell types. These results identify IL-4 as an additional cytokine
able to directly stimulate C2 production by human monocytes and
by a monocytic cell line whereas IL-4 stimulation of HLA-
DR expression by monocytes appears to be IFN-gamma dependent.

L4 ANSWER 62 OF 79 MEDLINE
DUPLICATE 38
ACCESSION NUMBER: 89291526 MEDLINE
DOCUMENT NUMBER: 89291526 PubMed ID: 2525543
TITLE: Alloactivated HLA class II-positive T-cell lines induce
IL-2 reactivity but lack accessory cell function in mixed
leukocyte culture.
AUTHOR: Odum N; Dickmeiss E; Hofmann B; Jakobsen B K; Morling N;
Platz P; Ryder L P; Geisler C; Svejgaard A
CORPORATE SOURCE: Department of Clinical Immunology, State University
Hospital, Copenhagen, Denmark.
SOURCE: HUMAN IMMUNOLOGY, (1989 Jun) 25 (2) 135-48.
Journal code: 8010936. ISSN: 0198-8859.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198908
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19890803

AB Recently, much interest has focused on the role of HLA class II antigens
in T cell-T cell interactions. We have studied the stimulatory capability
in the primary mixed leukocyte reaction and the primed lymphocyte reaction
of 11 alloactivated, HLA-DR- or -DP-reactive
CD4-positive T-cell lines (Ta). From 70 to 90% of the Ta were HLA class
II-positive as judged by the reactions with HLA class II-reactive
monoclonal antibodies, and the Ta carried the DR allospecificities of the
original T-cell donor when typed in the microcytotoxic test using
DR-specific alloantisera. Neither irradiated nor nonirradiated Ta
stimulated primed lymphocytes directed against the relevant HLA class II
antigens on the Ta. Interferon-gamma, recombinant
interleukin 1, phorbol myristate acetate, calcium ionophore, and adherent
cells had no effect on the stimulatory capability of Ta. The ability of
irradiated Ta to stimulate in the primary mixed leukocyte
reaction (median counts per minute (cpm) 5.5 x 10(3] was significantly
lower than that of peripheral blood mononuclear cells (cpm: 44.0 x 10(3].
The stimulation by Ta was almost only seen when the Ta were specifically

directed against the class II antigens of the responder peripheral blood
mononuclear cells (i.e., in combinations with "backstimulation") (median
cpm: 21,000). In mixed leukocyte reaction combinations without
backstimulation, significantly weaker reactions were seen (median cpm:
1,000). This observation may explain previous controversies concerning the
stimulatory capacity of Ta. Recombinant interleukin 2 significantly
enhanced the very low mixed leukocyte culture responses induced by class
II-incompatible Ta in combinations without backstimulation but had no
significant effect on cultures with Ta autologous to the responder
peripheral blood mononuclear cells. Thus, allogeneic class II-positive Ta
can induce interleukin 2 responsiveness but lack accessory cell
function(s) necessary for the induction of interleukin 2 production in
primed and unprimed T cells.

L4 ANSWER 63 OF 79 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1990:28160 BIOSIS
DOCUMENT NUMBER: BA89:15126
TITLE: INDUCTION OF CLASS II HISTOCOMPATIBILITY ANTIGENS HLA-DR ON CELLS OF HUMAN COLONIC EPITHELIUM UNDER THE INFLUENCE OF GAMMA INTERFERON AND OF LAMINA PROPRIA LYMPHOCYTES.
AUTHOR(S): RADWAN P; LOWES J; PRIDDLE J; JEWELL D
CORPORATE SOURCE: KLINIKA GASTROENTEROL. AKAD. MED. LUBLINIE, UL. JACZEWSKIEGO 8, 20-950 LUBLIN.
SOURCE: IMMUNOL POL, (1989) 14 (1), 37-44.
CODEN: IMPODM. ISSN: 0324-8534.
FILE SEGMENT: BA; OLD
LANGUAGE: Polish
AB Studies of expression of class II HLA antigens (HLA-DR
) by maintained in vitro colonic epithelial cells of neoplastic origin
were performed. The cells were exposed to various concentrations of gamma
interferon (.gamma. IFN) and to supernatants from
cultures of human lymphocytes isolated from lamina propria of normal colon
and of colon from unspecific intestinal inflammations (NZJ). Reaction was
evaluated qualitatively by immunohistochemical method with monoclonal
antibody anti HLA-DR and also quantitatively by
immunoenzymatic assay (micro-Elisa). It was found that both .gamma. IFN
and lymphokines produced by lamina propria lymphocytes induce HLA
-DR antigens on studied colonic epithelial cells. .gamma. IFN
was found to stimulate HLA-DR expression in
a dose independent way.

L4 ANSWER 64 OF 79 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1988:256670 BIOSIS
DOCUMENT NUMBER: BR34:127700
TITLE: HUMAN IL-4-BSF-1 STIMULATES C2 PRODUCTION AND HLA-DR EXPRESSION BY HUMAN MONOCYTES-MACROPHAGES.
AUTHOR(S): LITTMAN B H; CARLSON P L; SANDERS K M
CORPORATE SOURCE: MCGUIRE V.A. MED. CENT. AND MED. COLL. VIRGINIA, VA. COMM. UNIV., RICHMOND, VA. 23249.
SOURCE: 72ND ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, LAS VEGAS, NEVADA, USA, MAY 1-5, 1988. FASEB (FED AM SOC EXP BIOL) J, (1988) 2 (4), ABSTRACT 3447.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English

L4 ANSWER 65 OF 79 MEDLINE
DUPLICATE 39
ACCESSION NUMBER: 88203652 MEDLINE
DOCUMENT NUMBER: 88203652 PubMed ID: 2966398
TITLE: Calcium influx and the Ca2+-calmodulin complex are involved in interferon-gamma-induced expression of HLA class II molecules on HL-60 cells.
AUTHOR: Koide Y; Ina Y; Nezu N; Yoshida T O
CORPORATE SOURCE: Department of Microbiology and Immunology, Hamamatsu University School of Medicine, Japan.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1988 May) 85 (9) 3120-4.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198806
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19880609
AB Interferon gamma (IFN-gamma) induces HLA-DR and -DQ molecules and causes an accumulation of transcripts in
HL-60 cells. Experiments were, therefore, designed to investigate the
intracellular signaling molecules regulating the appearance of HLA class
II molecules. The expression of HLA class II (DR and DQ) molecules induced
by IFN-gamma was blocked by a calmodulin antagonist, W7, but not by a
protein kinase C inhibitor, H7. Furthermore, a direct activator of protein
kinase C, phorbol 12-myristate 13-acetate, was unable to induce HLA class
II (DR) molecule expression. These results suggest that IFN-gamma induces

HLA class II molecules on HL-60 cells by way of a calcium-calmodulin
pathway and not by way of a protein kinase C pathway. Calmodulin is
activated by a transient rise in the cytosolic free calcium. In fact,
IFN-gamma evoked a calcium influx into HL-60 cells, whereas depletion of
Ca2+ from culture medium resulted in a failure of IFN-gamma to induce DR
expression. Furthermore, the calcium ionophore A23187 by itself induced DR
molecule expression. These results suggest that IFN-gamma
stimulates calcium influx by a so-called receptor-mediated calcium
channel and activates the calmodulin branch of the calcium messenger
system, resulting in the induction of DR molecules on the surface of HL-60
cells.

L4 ANSWER 66 OF 79 MEDLINE
DUPLICATE 40
ACCESSION NUMBER: 88151077 MEDLINE
DOCUMENT NUMBER: 88151077 PubMed ID: 3125987
TITLE: Interferon gamma modulates the ability of autologous non-T cells to stimulate T cells to produce
and respond to interleukin 2.
AUTHOR: Kawano Y; Noma T; Itoh M; Yata J
CORPORATE SOURCE: Department of Pediatrics, National Defense Medical College,
Saitama, Japan.
SOURCE: CELLULAR IMMUNOLOGY, (1988 Mar) 112 (1) 166-73.
Journal code: 1246405. ISSN: 0008-8749.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198804
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19880412
AB The interactions of T-cell receptor with self-Ia antigen on non-T cells
induced IL-2 production and IL-2 receptors on the cell surface and thus
responsiveness to IL-2 of T cells in autologous mixed-lymphocyte reaction
(AMLR). Four-day-cultured autologous non-T cells lost their ability to
stimulate T cells to produce and respond to IL-2 with concurrent
decrease of HLA-DR and HLA-DQ antigen expressed on the
cell surface. Culturing of non-T cells with 500 U/ml of recombinant
interferon gamma (IFN-gamma) maintained their
stimulating ability which was otherwise lost. Treatment of non-T cells
with monoclonal anti-HLA-DR or anti-HLA-DQ antibody
before mixture with T cells abrogated their ability to induce IL-2
production and IL-2 responsiveness of T cells. The combined data suggested
that Ia antigen expressed on non-T cells is modulated by IFN-gamma, which
increases the ability of non-T cells to stimulate autologous T
cells to produce and respond to IL-2.

L4 ANSWER 67 OF 79 MEDLINE
DUPLICATE 41
ACCESSION NUMBER: 88210483 MEDLINE
DOCUMENT NUMBER: 88210483 PubMed ID: 3130193
TITLE: Interleukin-2-induced production of interferon-
gamma by resting human T cells and large granular
lymphocytes: requirement for accessory cell factors,
including interleukin-1.
AUTHOR: Wilson A B; Harris J M; Coombs R R
CORPORATE SOURCE: Department of Pathology, University of Cambridge, England.
SOURCE: CELLULAR IMMUNOLOGY, (1988 Apr 15) 113 (1) 130-42.
Journal code: 1246405. ISSN: 0008-8749.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198806
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19880614
AB Between 5 and 20% of normal human lymphocytes were found to synthesize
interferon-gamma (IFN-gamma) in primary cultures with
recombinant interleukin-2 (rIL-2). After 22 hr, IFN-gamma-producing cells
included CD5+ T lymphocytes, CD16+ large granular lymphocytes (LGL), and a
population of CD5-, CD16- blast cells. Only a small proportion (0-7%) of
IFN-gamma-synthesizing cells expressed HLA-DR. The
production of IFN-gamma by all rIL-2-responding lymphocyte subsets was
shown to require the presence of DR+ accessory cells, probably including
nonadherent, esterase-negative monocytes and/or dendritic cells. Accessory
cell function in lymphocyte preparations depleted of DR+ cells, or in
purified (greater than or equal to 95%) suspensions of LGL, was fully
replaced either by addition of 2% autologous, adherent monocytes or by
monocyte culture supernatant. The activity of monocyte supernatant was
greatly reduced by treatment with antiserum specific for human
interleukin-1 beta (IL-1 beta), although a combination of rIL-1 beta and
rIL-2 failed to stimulate IFN-gamma production in DR-
lymphocytes. These results indicate that rIL-2-induced IFN-gamma synthesis
in both T cells and LGL requires the synergistic activity of IL-1, and

possibly of one or more other monokines, as yet unidentified.

L4 ANSWER 68 OF 79 MEDLINE
DUPLICATE 42
ACCESSION NUMBER: 88269840 MEDLINE
DOCUMENT NUMBER: 88269840 PubMed ID: 2455573
TITLE: Enhancement of release from MHC class II antigen-positive monocytes of hematopoietic colony stimulating factors CSF-1 and G-CSF by recombinant human tumor necrosis factor-alpha: synergism with recombinant human interferon-gamma.
AUTHOR: Lu L; Walker D; Graham C D; Waheed A; Shadduck R K; Broxmeyer H E
CORPORATE SOURCE: Department of Medicine, Indiana University School of Medicine, Indianapolis 46223.
CONTRACT NUMBER: CA 15237 (NCI)
CA 36464 (NCI)
CA 36740 (NCI)
SOURCE: BLOOD, (1988 Jul) 72 (1) 34-41.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198808
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19880819
AB The influence of purified recombinant human tumor necrosis factor-alpha (rhuTNF-alpha) was assessed alone and in combination with purified recombinant human interferon gamma (rhuIFN-gamma) for its effects on enhancing release from human monocytes of activities that stimulate colony formation by granulocyte-macrophage (CFU-GM), erythroid (BFU-E), and multipotential (CFU-GEMM) progenitor cells. RhuTNF-alpha or rhuIFN-gamma enhanced release of colony stimulating factors (CSFs), which were determined by a combination of human and mouse colony assays, morphological assessment of colony types and neutralization studies with anti-human macrophage CSF (CSF-1) and anti-human granulocyte (G)-CSF to be CSF-1 and G-CSF. The activity in the uninduced and induced monocyte conditioned media (CM) for CFU-GM-type colonies and clusters was attributed to the presence of both CSF-1 and G-CSF, while the activity in the monocyte CM for BFU-E and CFU-GEMM colonies was attributed to the presence of G-CSF. Monocytes were separated by two-color fluorescence using a dye laser flow cytometry system with cells labeled with anti-leu M3 conjugated with fluorescein isothiocyanate and anti-HLA-DR conjugated with phycoerythrin. While "constitutive" release of CSFs from monocytes was apparent from both the leu M3+, HLA-DR+ and the leu M3+, HLA-DR- (low density or negative DR) fractions, enhanced release of CSFs in response to rhuTNF-alpha or rhuIFN-gamma was confined to the leu M3+, HLA-DR+ population of cells. RhuTNF-alpha and rhuIFN-gamma synergized to enhance release of CSFs such that low concentrations of each molecule, which were inactive when used alone, were active when the two molecules were used together. These studies suggest a role, at least in vitro, for TNF-alpha and IFN-gamma in the release of CSFs from cells of the mononuclear phagocytic lineage.

L4 ANSWER 69 OF 79 CANCERLIT
ACCESSION NUMBER: 89650502 CANCERLIT
DOCUMENT NUMBER: 89650502
TITLE: INTERFERON EFFECTS ON CELLULAR AND HUMORAL IMMUNITY.
AUTHOR: De Maeyer E; De Maeyer-Guignard J
CORPORATE SOURCE: Institut Curie-Biologie, Bat. 110, Campus d'Orsay, 91405 Orsay, France.
SOURCE: Non-serial, (1987) The Interferon System. A Current Review to 1987. Baron S et al, eds. The University of Texas Medical Branch Series in Biomedical Science, Austin, TX, University of Texas Press, p. 327-35, 1987.
DOCUMENT TYPE: Book; (MONOGRAPH)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Institute for Cell and Developmental Biology
ENTRY MONTH: 198904
ENTRY DATE: Entered STN: 19941107
Last Updated on STN: 19960517
AB Results of recent studies on effects of interferons (IFNs) on cellular and humoral immunity are reviewed under the following headings: expression of cell surface molecules--antigens and receptors (antigens of the major histocompatibility complex [MHC], effects on other cell surface molecules), interaction with interleukin 2 (IL2), macrophage activation, and effects on B cells. It was previously shown that recombinant human IFN-gamma (rHuIFN-gamma) can increase the synthesis and expression of the Class II MHC antigens, HLA-DR, on human monocytes; recent evidence indicates that rHuIFN-gamma also induces the expression of Class II antigens HLA-DR and HLA-DC on tumor cells of

various origins, such as melanoma cells, glioma cells, and cells from
several human carcinoma lines. Normal fibroblasts also can express Class
II antigens when induced with IFN-gamma. In addition, IFN-gamma has been
shown to modulate Class II HLA antigen expression on cultured thymic
epithelial cells, and this finding raises the possibility that IFN-gamma
participates in mechanisms that assure the permanent expression of these
antigens on thymic epithelial cells in vivo. IFN-gamma is the prime
inducer of expression of Class II antigens, while IFN-alpha and -beta play
only secondary roles in this respect; however, expression of Class I
antigens is usually readily induced by all three IFN species. Class I HLA
cell lines having high or low responses to HuIFN-alpha have been isolated
from the human thymus leukemia cell line Molt 4. A natural role for
HuIFN-beta in the turning on of Class I HLA antigens during cell
differentiation was strongly suggested by experiments, in which the
appearance of Class I antigens during differentiation of cells of a
lymphoma line to macrophages was inhibited by treatment with anti-IFN-beta
serum. This observation points to IFNs as natural modulators during the
normal differentiation process of cells derived from the hematopoietic
system. Enhanced expression of histocompatibility antigens is but one
manifestation of the ability of IFNs to stimulate the expression
of genes coding for cell-surface molecules important for immune reactions;
eg, the number of cellular receptors for tumor necrosis factor is
significantly enhanced by treatment with IFN-gamma and, to a lesser
extent, with IFN-alpha and -beta. Other cell surface receptor molecules
influenced by IFN-gamma treatment are IL2 receptors on human peripheral
blood monocytes, which are enhanced, and transferrin receptors on murine
peritoneal macrophages, which are downregulated. Finally, interactions of
IFNs with IL2, macrophage activation by IFNs, and effects of IFN-gamma on
B cells are reviewed. (64 Refs)

L4 ANSWER 70 OF 79 MEDLINE
DUPLICATE 43
ACCESSION NUMBER: 88024285 MEDLINE
DOCUMENT NUMBER: 88024285 PubMed ID: 3117066
TITLE: Effects of gold sodium thiomalate on interferon stimulation
of C2 synthesis and HLA-DR expression by human monocytes.
AUTHOR: Sanders K M; Carlson P L; Littman B H
CORPORATE SOURCE: Department of Medicine, Medical College of Virginia,
Virginia Commonwealth University, Richmond.
CONTRACT NUMBER: 5-732-CA 09210-08 (NCI)
SOURCE: ARTHRITIS AND RHEUMATISM, (1987 Sep) 30 (9) 1032-9.
Journal code: 0370605. ISSN: 0004-3591.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198711
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19970203
Entered Medline: 19871104
AB Gamma-interferon (gamma-IFN) is a T cell-derived lymphokine that has potent macrophage-activating properties. It increases
Fc receptor density, increases the formation and release of reactive
oxygen intermediates, increases the synthesis and release of complement
cascade proteins, especially C2 and factor B, and increases class II (
HLA-DR) antigen expression. These effects may play a
role in the potentiation of inflammation in rheumatoid arthritis. We
examined the possibility that gold sodium thiomalate (GST), an effective
treatment for rheumatoid arthritis, would inhibit gamma-IFN-mediated
stimulation of monocyte/macrophages. GST in concentrations attainable in
vivo was shown to inhibit both spontaneous and gamma-IFN-stimulated C2
production up to 50%. GST inhibition could be only partially overcome with
increasing concentrations of gamma-IFN. In addition, GST inhibited
gamma-IFN-stimulated HLA-DR expression at the highest
concentrations tested (20-50 micrograms/ml). GST alone in low
concentrations (0.1-5 micrograms/ml) was found to increase HLA-
DR antigen expression as quantitated by several methods, including
flow cytometry, cell surface enzyme-linked immunosorbent assay, and
Western blotting. This GST-stimulated increase in HLA-DR
antigen expression paralleled an increased ability of monocytes to present
antigen. The mechanism by which low concentrations of GST
stimulate HLA-DR antigen expression is
unclear, but was shown by 35S-methionine cell labeling not to involve
increased HLA-DR protein synthesis.

L4 ANSWER 71 OF 79 MEDLINE
DUPLICATE 44
ACCESSION NUMBER: 87252239 MEDLINE
DOCUMENT NUMBER: 87252239 PubMed ID: 3110281

TITLE: Differential presentation of HLA-DR, DQ, and DP restriction
elements by interferon-gamma-treated dermal fibroblasts.
AUTHOR: Maurer D H; Hanke J H; Mickelson E; Rich R R; Pollack M S
CONTRACT NUMBER: AI15394 (NIAID)
AM33988 (NIADDK)
CA40552 (NCI)
+
SOURCE: JOURNAL OF IMMUNOLOGY, (1987 Aug 1) 139 (3) 715-23.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198708
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19970203
Entered Medline: 19870826
AB IFN-gamma has been reported to induce expression of HLA class II (DR, DQ,
DP) antigens on cultured human dermal fibroblasts (FB) by stimulating the
de novo transcription of the alpha and beta chain genes of HLA-
DR, -DQ, and -DP in these cells. We examined the relative nominal
and alloantigen-presentation capacity of each HLA class II gene product on
FB by using CD4-positive, TNP-specific T cell clones restricted by
determinants on DR, DQ, or DP molecules, as well as allospecific,
CD4-positive T cell clones recognizing DR-, DQ-, or DP-lymphocyte
activating determinants. After IFN-gamma exposure, FB strains used for
antigen presentation displayed a high percentage of DR-positive cells and
a much smaller percentage of DP-positive cells, but no detectable
DQ-positive cells by immunofluorescent techniques. FB stimulator cells
supported proliferative responses of two DR-allospecific T cell clones and
one TNP-specific, DR-restricted clone, but not another TNP-specific,
DR-restricted clone. Despite only modest DP expression, FB stimulated both
a TNP-specific, DP-restricted clone and a DP-allospecific T cell line.
However, IFN-gamma treated FB failed to stimulate a
TNP-specific, DQ-restricted clone and a DQ-allospecific clone. Our data
indicate that IFN-gamma differentially regulates expression of functional
class II lymphocyte activating determinants on FB antigen-presenting cells
and that FB may fail to support DQ-directed T cell responses due to
insufficient expression of DQ molecules on the FB cell surface. However,
the quantity of DR or DP expressed on FB did not directly correlate with
their ability to support T cell responses, indicating that additional
factors, such as differences in T cell clone activation requirements,
contribute to the capacity of FB to present class II allo- and
antigen-restricting epitopes.

L4 ANSWER 72 OF 79 MEDLINE
DUPLICATE 45
ACCESSION NUMBER: 87084761 MEDLINE
DOCUMENT NUMBER: 87084761 PubMed ID: 3098840
TITLE: Dissection of defective antigen presentation by
interferon-gamma-treated fibroblasts.
AUTHOR: Geppert T D; Lipsky P E
CONTRACT NUMBER: AM-09989 (NIADDK)
SOURCE: JOURNAL OF IMMUNOLOGY, (1987 Jan 15) 138 (2) 385-92.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198702
ENTRY DATE: Entered STN: 19900302
Last Updated on STN: 19970203
Entered Medline: 19870218
AB The capacity of interferon-gamma (IFN-gamma)-treated
HLA-DR expressing human dermal fibroblasts (FB) to
function as antigen-presenting cells (APC) was examined. FB were cultured
with 250 U/ml IFN-gamma for 4 days to induce HLA-DR
expression. Peripheral blood monocytes (M phi), FB, or IFN-gamma-treated
FB from the same donor were then cultured overnight with or without the
recall antigen streptokinase streptodornase (SKSD), and their capacity to
stimulate autologous T4 cell DNA synthesis was examined.
SKSD-bearing M phi stimulated T4 cell proliferation, whereas
antigen-bearing HLA-DR (+) FB did not. Even after
fixation with paraformaldehyde to eliminate metabolic activity,
SKSD-bearing M phi, but not FB, were able to function as APC. However,
when HLA-DR (-) endothelial cell (EC) or autologous or
HLA-D-mismatched M phi were added to the cultures, antigen-pulsed
IFN-gamma-treated FB and M phi were comparably effective stimulators of
autologous T4 cell DNA synthesis. Antigen recognition by the T4 cell was
restricted by the class II major histocompatibility complex (MHC)-encoded
gene products expressed by the IFN-gamma-treated FB and was unrelated to
the class I or II MHC-encoded gene products expressed by the additional

cell type. EC-promoted T4 cell DNA synthesis induced by antigen-bearing
IFN-gamma-treated FB was inhibited by 60.3, a monoclonal antibody directed
at an epitope common to LFA-1, CR3, and the p150,95 molecule. Inhibition
caused by 60.3 was completely reversed by the addition of IL 2 to the
cultures. Antigen presentation by IFN-gamma-treated FB was also enhanced
somewhat by IL 1, IL 2, or monoclonal antibody directed at Tp44 (9.3).
However, each of these additions alone promoted T cell proliferation less
effectively than EC and resulted in responses that were smaller than those
triggered by antigen-bearing M phi. The data suggest that
IFN-gamma-treated FB take up and process antigen effectively, but lack an
accessory cell property necessary for antigen-induced T4 cell IL 2
production and proliferation.

L4 ANSWER 73 OF 79 MEDLINE
DUPLICATE 46
ACCESSION NUMBER: 87224172 MEDLINE
DOCUMENT NUMBER: 87224172 PubMed ID: 3108402
TITLE: Interferon-gamma regulates the T cell response to precursor nevi and biologically early melanoma.
AUTHOR: Guerry D 4th; Alexander M A; Elder D E; Herlyn M F
CONTRACT NUMBER: CA 25874 (NCI)
CA 29200 (NCI)
CA25298 (NCI)
SOURCE: JOURNAL OF IMMUNOLOGY, (1987 Jul 1) 139 (1) 305-12.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198707
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19970203
Entered Medline: 19870723
AB To examine the potential regulatory role of interferon-
gamma in the cellular immune response to melanoma and its
precursor lesions, we have tested the capacity of this lymphokine to
enhance HLA class II antigen-dependent T lymphocyte blastogenesis, its in
vitro production by autologous T cells stimulated by melanoma, and its
presence in melanocytic lesions in situ. Cell lines derived from a
dysplastic nevus, a radial growth phase primary tumor, a vertical growth
phase primary, and metastatic lesions were induced by recombinant
interferon-gamma to express increased amounts of HLA
class II antigens. Such cells were then examined in radioimmunoassay for
expression of HLA-DR antigens and in co-culture for
their ability to stimulate proliferation of autologous T cells.
Interferon-gamma treatment of melanocytic cells
increased their expression of HLA-DR antigens
threefold to sixfold. In parallel with these findings, co-culture of T
cells with interferon-treated cells of a dysplastic nevus and a radial
phase melanoma led to augmented T cell incorporation of tritiated
thymidine, and this stimulation was inhibited with a monoclonal antibody
to HLA-DR antigens. Despite augmented expression of
HLA class II antigens (HLA-DR, -DQ, and -DP), vertical
growth phase and metastatic melanoma cells failed to stimulate
autologous T cells. When T cells were co-cultured with stimulating
melanoma cells, culture supernatants contained significantly increased
amounts of interferon-gamma (12 U/ml) in comparison
with supernatants of T cells alone (4 U/ml). No interferon was detectable
in cultures of melanoma cells alone. To link these in vitro phenomena to
in situ events, we used murine monoclonal antibodies to interferon
-gamma, the interleukin 2 receptor, and HLA-DR
antigens in an immunoperoxidase system to detect interferon production and
lymphocyte activation in frozen sections of lesions representative of
melanocytic tumor progression. In these studies, precursor dysplastic nevi
and radial phase melanomas contained the highest numbers of activated
lymphocytes and stained positively for interferon-gamma
. These results suggest that interferon-gamma plays a
central role in the regulation of the cellular immune response to
melanoma. It is produced by T cells, likely activated by tumor antigens
seen in the context of HLA class II antigens. In turn, interferon
-gamma production enhances expression of HLA class II antigens
by melanoma and precursor cells, and such enhancement is associated with
additional T cell activation in a positive feed-back loop.

L4 ANSWER 74 OF 79 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 87159300 EMBASE
DOCUMENT NUMBER: 1987159300
TITLE: Interferon-.gamma. regulates the T cell response to precursor nevi and biologically early melanoma.
AUTHOR: Guerry IV D.; Alexander M.A.; Elder D.E.; Herlyn M.F.
CORPORATE SOURCE: Pigmented Lesion Study Group, The Hematology-Oncology

Section, Department of Medicine, University of Pennsylvania
School of Medicine, Philadelphia, PA, United States
SOURCE: Journal of Immunology, (1987) 139/1 (305-312).
CODEN: JOIMA3
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
016 Cancer
LANGUAGE: English
AB To examine the potential regulatory role of interferon-.
gamma. in the cellular immune response to melanoma and its
precursor lesions, we have tested the capacity of this lymphokine to
enhance HLA class II antigen-dependent T lymphocyte blastogenesis, its in
vitro production by autologous T cells stimulated by melanoma, and its
presence in melanocytic lesions in situ. Cell lines derived from a
dysplastic nevus, a radial growth phase primary tumor, a vertical growth
phase primary, and metastatic lesions were induced by recombinant
interferon-.gamma. to express increased amounts of HLA
class II antigens. Such cells were then examined in radioimmunoassay for
expression of HLA-DR antigens and in coculture for
their ability to stimulate proliferation of autologous T cells.
Interferon-.gamma. treatment of melanocytic cells
increased their expression of HLA-DR antigens
threefold to sixfold. In parallel with these findings, co-culture of T
cells with interferon-treated cells of a dysplastic nevus and a radial
phase melanoma led to augmented T cell incorporation of tritiated
thymidine, and this stimulation was inhibited with a monoclonal antibody
to HLA-DR antigens. Despite augmented expression of
HLA class II antigens (HLA-DR, -DQ, and -DP), vertical
growth phase and metastatic melanoma cells failed to stimulate
autologous T cells. When T cells were co-cultured with stimulating
melanoma cells, culture supernatants contained significantly increased
amounts of interferon-.gamma. (12 U/ml) in comparison
with supernatants of T cells alone (4 U/ml). No interferon was detectable
in cultures of melanoma cells alone. To link these in vitro phenomena to
in situ events, we used murine monoclonal antibodies to interferon
-.gamma., the interleukin 2 receptor, and HLA-
DR antigens in an immunoperoxidase system to detect interferon
production and lymphocyte activation in frozen sections of lesions
representative of melanocytic tumor progression. In these studies,
precursor dysplastic nevi and radial phase melanomas contained the highest
numbers of activated lymphocytes and stained positively for
interferon-.gamma.. These results suggest that
interferon-.gamma. plays a central role in the
regulation of the cellular immune response to melanoma. It is produced by
T cells, likely activated by tumor antigens seen in the context of HLA
class II antigens. In turn, interferon-.gamma.
production enhances expression of HLA class II antigens by melanoma and
precursor cells, and such enhancement is associated with additional T cell
activation in a positive feed-back loop.

L4 ANSWER 75 OF 79 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1987:526636 CAPLUS
DOCUMENT NUMBER: 107:126636
TITLE: Augmentation by an organic germanium compound Ge-132
of HLA-DR antigen- and IgG-Fc receptor-expression on
human macrophages
AUTHOR(S): Hanaumi, Kiyoshi; Kumagai, Katsuo
CORPORATE SOURCE: Sch. Dent., Tohoku Univ., Sendai, Japan
SOURCE: Ensho (1987), 7(3), 253-8
CODEN: ENSHEE; ISSN: 0389-4290
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Ge-132 (carboxyethylgermanium sesquioxide) added in the cultures of either
purified peripheral monocytes or U937 human myelogenous leukemia cells did
not produce any significant effect on expression of either HLA-DR antigens
or FcR1 on the cell. Incubation of peripheral blood mononuclear cells
(PBMC) with Ge-132, however, produced a factor inducing augmentation of
HLA-DR and IgG-Fc receptor (FcR1) expression on the monocytes or U937.
Pretreatment of this PBMC culture fluid with pH 2.0 or specific antiserum
against human interferon .gamma.(IFN.gamma.) resulted
in a marked redn. of both HLA-DR and FcR-inducing activities, suggesting
that a major factor induced by Ge-132 in the PBMC may be IFN.gamma..
Ge-132 may stimulate PBMC to produce a sol. factor (IFN.gamma.),
which in turn augments the expression of HLA-DR
antigens and FcR1 on the cell of myelogenous or macrophage series.

L4 ANSWER 76 OF 79 MEDLINE
DUPLICATE 47
ACCESSION NUMBER: 87035442 MEDLINE
DOCUMENT NUMBER: 87035442 PubMed ID: 2430045

TITLE: Production of a cytokine with interleukin 3-like properties
and cytokine-dependent proliferation in human autologous
mixed lymphocyte reaction.
AUTHOR: Suzuki R; Suzuki S; Takahashi T; Kumagai K
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1986 Nov 1) 164 (5)
1682-99.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198612
ENTRY DATE: Entered STN: 19900302
Last Updated on STN: 19900302
Entered Medline: 19861203
AB The autologous mixed lymphocyte reaction (AMLR) was assayed in a medium
containing fresh autologous serum, by using nylon-adherent stimulator
cells and nonadherent responder T cells, which were prepared from human
peripheral blood mononuclear cells in the absence of fetal calf serum
(FCS) to avoid any sensitization to xenogeneic protein antigens. DNA
replication without a background proliferative response was induced by
stimulator cells in the responder cells. The addition of monoclonal anti-
HLA-DR antibody to the culture or treatment of the
responder cells with complement plus anti-T4 but not anti-T8 monoclonal
antibody suppressed the AMLR, suggesting that this specific AMLR involves
an interaction between HLA-DR antigens and
helper/inducer T cells. Regardless of this specific DNA replication, the
AMLR generated no production of interleukin 2 (IL-2) and
interferon gamma (IFN-gamma), both of which could be
found in the allogeneic (allo) MLR. In addition, DNA replication in the
AMLR was not inhibited by the addition of specific antisera for IL-2 and
IFN-gamma, both of which significantly inhibited the DNA replication in
allo-MLR. The AMLR was accompanied by production of a soluble factor,
which could stimulate the proliferation of murine interleukin 3
(IL-3)-dependent cell line 32Dcl but not the proliferation of
IL-2-dependent cell lines. This factor was also found to be responsible
for proliferation of responder nonadherent cells in the AMLR. It strongly
stimulated bone marrow cells, as did the murine IL-3. The factor had an Mr
range, as determined by gel filtration, of 15,000-28,000, but it did not
bind to fast protein liquid chromatography (FPLC)-MonoQ column. Thus, the
factor is distinguishable from IL-2 in physicochemical or biological
properties, but similar to murine IL-3. These results suggest that the
human AMLR may be primarily a phenomenon in which non-T cells mediated by
the HLA-DR antigens on the cell stimulate
helper/inducer T cells to produce a lymphokine with IL-3-like properties,
but no IL-2, which in turn stimulates the factor-dependent cells
to proliferate.

L4 ANSWER 77 OF 79 MEDLINE
DUPLICATE 48
ACCESSION NUMBER: 86087152 MEDLINE
DOCUMENT NUMBER: 86087152 PubMed ID: 3484491
TITLE: Antigen presentation by human dermal fibroblasts:
activation of resting T lymphocytes.
AUTHOR: Umetsu D T; Katzen D; Jabara H H; Geha R S
CONTRACT NUMBER: AI20373 (NIAID)
AI21163 (NIAID)
AM31925 (NIADDK)
+
SOURCE: JOURNAL OF IMMUNOLOGY, (1986 Jan) 136 (2) 440-5.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198602
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19860205
AB We have shown that human dermal fibroblasts, exposed to interferon
-gamma (IFN-gamma) to induce surface class II major
histocompatibility complex (MHC) antigens, were capable of presenting
tetanus toxoid (TT) antigen to human TT-specific T cell clones. Antigen
presentation by fibroblasts was antigen dependent, required HLA-
DR expression by fibroblasts, and was MHC restricted. In contrast,
we now report that IFN-gamma-treated fibroblasts are unable to present TT
antigen to purified resting T cells obtained from the peripheral blood of
TT-immune donors. In addition, although IFN-gamma-treated fibroblasts were
able to stimulate alloreactive T cell clones, they were unable
by themselves to stimulate primary allogeneic responses in
resting T cells. The failure of fibroblasts to stimulate resting
T cells was not due to suppressor effects by fibroblasts, because
induction of TT and alloantigen responses in resting T cells by monocytes

was not inhibited by the presence of fibroblasts. On the contrary,
IFN-treated fibroblasts were synergistic with small numbers of monocytes
in activating resting T cells. In addition, the failure of antigen
presentation by fibroblasts to resting T cells was reversed by the
addition of recombinant human interleukin 2 (rIL 2) to cultures, but not
of purified human interleukin 1 (IL 1). These results emphasize that the
requirements for activation of resting T cells differ from those of T cell
clones. Although fibroblasts can efficiently present antigen to T cell
clones, antigen presentation by fibroblasts to resting T cells requires
the addition of exogenous IL 2. It is postulated that fibroblasts differ
from classical antigen-presenting cells in that fibroblasts are incapable
of stimulating the production of IL 2 in resting T cells.

L4 ANSWER 78 OF 79 MEDLINE
DUPLICATE 49
ACCESSION NUMBER: 86060842 MEDLINE
DOCUMENT NUMBER: 86060842 PubMed ID: 3934267
TITLE: Antigen presentation by interferon-gamma
-treated endothelial cells and fibroblasts: differential
ability to function as antigen-presenting cells despite
comparable Ia expression.
AUTHOR: Geppert T D; Lipsky P E
CONTRACT NUMBER: AM09989 (NIADDK)
SOURCE: JOURNAL OF IMMUNOLOGY, (1985 Dec) 135 (6) 3750-62.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198512
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19851223
AB The effect of interferon-gamma (IFN-gamma) on
endothelial cell (EC) and fibroblast (FB) class II major
histocompatibility complex (MHC) gene product expression and antigen
presenting ability was examined. Control FB did not express class II MHC
gene products, whereas a small (less than 1%) population of passaged EC
expressed class II gene products. IFN-gamma induced a comparable density
of HLA-DR expression on nearly all EC and FB.
IFN-gamma-treated EC and FB also expressed HLA-DP but at a lower density,
whereas HLA-DQ expression was barely detectable on either cell type.
Control FB were not able to stimulate allogeneic T4 cell DNA
synthesis or function as antigen-presenting cells (APC). Control EC were
also unable to stimulate allogeneic T4 cell DNA synthesis unless
large numbers of stimulator cells were used. Small numbers of
IFN-gamma-treated EC were able to stimulate allogeneic T4 cell
DNA synthesis, whereas larger numbers were markedly more effective than
control EC. In contrast, IFN-gamma-treated FB were ineffective stimulators
of allogeneic T4 cell DNA synthesis. IFN-gamma-treated FB were able to
present the exogenous antigen SKSD to autologous but not allogeneic T4
cells, but they were extremely inefficient APC. The inability of
IFN-gamma-treated FB to function as APC could not be explained by
FB-mediated immunosuppression, Ia density, or HLA-DQ expression. This
limited capacity of IFN-gamma-treated FB to participate in Ia-restricted
functional interactions with T4 cells correlated with a similar diminished
capacity to support nonspecific mitogen-induced proliferation of T4 cells
before IFN-gamma-induced Ia expression. This accessory cell function was
not enhanced by IFN-gamma treatment. Monocytes syngeneic to the responding
T4 cells but not interleukin 1 (IL 1) permitted IFN-gamma-treated FB but
not control FB to stimulate allogeneic T4 cell DNA synthesis,
but they remained markedly less effective stimulators than monocytes.
Moreover, IFN-gamma-treated FB were effective stimulators of alloprimed T4
cells, in contrast to their inability to stimulate fresh T4
cells. Furthermore, monocytes and IFN-gamma-treated FB were comparably
effective stimulators of alloreactive T cell lines. These data suggest
that accessory cells perform functions unrelated to Ia and IL 1 that are
necessary for mitogen-, alloantigen-, and antigen-induced proliferation of
freshly isolated T cells. Monocytes and EC effectively perform this
function, but FB do not. This accessory cell function does not seem to be
as important for the activation of primed T cells.

L4 ANSWER 79 OF 79 MEDLINE
DUPLICATE 50
ACCESSION NUMBER: 84112763 MEDLINE
DOCUMENT NUMBER: 84112763 PubMed ID: 6420462
TITLE: Interferons as modulators of human monocyte-macrophage
differentiation. I. Interferon-gamma
increases HLA-DR expression and inhibits phagocytosis of
zymosan.
AUTHOR: Becker S
CONTRACT NUMBER: CA29589 (NCI)
CA33003 (NCI)

SOURCE: JOURNAL OF IMMUNOLOGY, (1984 Mar) 132 (3) 1249-54.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198403
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19840323

AB The development of HLA-DR (Ia) expression in the presence and absence of interferon-gamma was monitored in monocyte-macrophage cultures. Overnight incubation with doses as low as 5 U/ml gave elevated values for Ia expression and the maximum increase was obtained with 200 U/ml. In contrast interferon-alpha had only a slight effect on the expression of Ia at doses as high as 2000 U/ml. The increase seen at 24 hr was maintained during the first 2 days of culture. The interferon-gamma-treated cells expressed four to five times more Ia than fresh monocytes. During the same time, monocytes cultured in the absence of interferon expressed approximately two times the amount of fresh monocytes. When the surface density of Ia was calculated, the interferon-gamma-treated monocytes expressed twice that of the untreated cells. Major changes in morphology and size occurred between days 3 and 4 of monocyte to macrophage development. Consequently a rapid increase in Ia expression took place; however, when the surface density was calculated this value increased only slightly when the monocytes matured to macrophages. The interferon -gamma-treated cells continued to express more total Ia as well as having increased surface density of this antigen. Interferon-gamma was also added to monocyte-macrophages several days after culture initiation (days 3, 4, and 5). Despite being in different stages of maturation, the cells responded to the interferon with increased Ia expression and surface density. The phagocytic activity of opsonized zymosans was also monitored. In contrast to Ia expression, this activity was downregulated by interferon-gamma, and the lower levels of phagocytosis were maintained through the 7 days of observation. Thus, interferon-gamma appears to change the differentiation pathway of the monocyte. The signal stimulates an increased level of Ia that may assist in the initiation of immune responses, and at the same time downregulates the scavenger role of removing opsonized particles. Once the monocyte has received this specific signal it continues to develop in a pathway different from that of the nontreated monocytes.

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